

**ERYTHRASMA – A CLINICAL STUDY AND A
COMPARATIVE STUDY OF TOPICAL
2% CLOTRIMAZOLE CREAM VS TOPICAL 2%
FUSIDIC ACID CREAM IN ITS TREATMENT**

Dissertation Submitted to

THE TAMIL NADU DR.MGR MEDICAL UNIVERSITY

partial fulfillment of the university regulations

for the award of degree of

M.D. (Dermatology, Venereology and Leprosy)

BRANCH - XX



CHENGALPATTU MEDICAL COLLEGE

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI, INDIA

APRIL 2016

DECLARATION

I, **DR.PRATHYUSHA PRABHAKAR**, solemnly declare that dissertation titled, “**ERYTHRASMA – A CLINICAL STUDY AND A COMPARATIVE STUDY OF TOPICAL 2% CLOTRIMAZOLE CREAM VS 2% FUSIDIC ACID CREAM IN ITS TREATMENT**” is a bonafide work done by me at Chengalpattu Medical College during 2013-2016 under the guidance and supervision of **Prof.Dr.O.H.Hema MD, DD.,** Professor and Head, Department of Dermatology, Venereology and Leprosy, Chengalpattu Medical College, Chengalpattu. This dissertation is submitted to The Tamil Nadu Dr.M.G.R.Medical University, towards partial fulfillment of requirement for the award of **M.D. (Dermatology, Venereology and Leprosy) (BRANCH –XX)**

Signature of the guide

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Place : Chengalpattu

Date :

CERTIFICATE

Certified that this dissertation entitled "**ERYTHRASMA - A CLINICAL STUDY AND A COMPARATIVE STUDY OF TOPICAL 2% CLOTRIMAZOLE VS 2% FUSIDIC ACID CREAM IN THE TREATMENT**" is a bonafide work done by **Dr.Prathyusha Prabhakar**, post graduate student of the Department of Dermatology,Venereology and Leprosy, Chengalpattu medical college during the academic year 2013 - 2016. This work has not previously formed the basis for the award of any degree or diploma.

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APPROVAL OF ETHICAL COMMITTEE

To

Dr.Prathyusha Prabhakar
Post Graduate
Dept of Dermatology

Dear Dr.

The Institutional Ethical Committee of Chengalpattu Medical College reviewed and discussed your application to conduct the clinical / dissertation work entitled

ERYTHRASMA - A CLINICAL STUDY AND A COMPARATIVE STUDY OF TOPICAL CLOTRIMAZOLE VS TOPICAL FUSIDIC ACID IN THE TREATMENT OF ERYTHRASMA

On 13.11.2013

The following documents reviewed

- a. Trial protocol, dated _____ version no
- b. Patient information sheet and informed consent form in English and / or vernacular language.
- c. Investigators Brochure, dated _____ version
- d. Principal Investigators current CV
- e. Investigators undertaking

The following members of the Ethics committee were present at the meeting held on

Date 13.11.2013 Time 12.00 Noon Place Chengalpattu Medical College

Approved J. Ravi Chairman Ethics Committee

By [Signature] 13/11/13 Member secretary of Ethics Committee.

Prathyusha
4/11/15

Name of each member with designation

Clinical Members

1. Dr.G.Raja Billy Graham MS.,
Prof & HOD of Surgery, CHMC
2. Dr.K.Srinivasagalu MD.,
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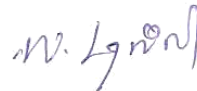
Biological Scientist

3. Dr.K.Baskaran MD.,
Asso Prof of Pharmacology, CHMC



Non Clinical Members

4. Dr.P.Parasakthi MD
Prof & HOD of Forensic Medicine, CHMC
5. Member from Nongovernmental
Voluntary Organisation : Mr.P.Durairaj
6. Philosopher : Mr.K.S.Ramprasad
7. Lawyer : Lr. I. M. Karimala Basha
8. Layperson : Mr.Dilli



We approve the clinical trial to be conducted in its presented form

The Institutional Ethics Committee expects to be informed about the progress of the study and any SAE occurring in the course of the study, any changes in protocol and patient information / informed consent and asks to provide copy of final report.

Yours sincerely



13/11/13
Member secretary, Ethics Committee

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ABSTRACT

AIM :

To study the clinical profile of erythrasma and to compare the effectiveness of 2% topical clotrimazole cream vs 2% topical fusidic acid cream in its treatment.

MATERIAL AND METHODS:

A randomised prospective, open labeled clinical study and a comparative study of 1 year (Jan 2014-Jan 2015) duration was conducted in 50 patients who were attending the dermatology outpatient department of Chengalpattu Medical College satisfying the inclusion and exclusion criteria after obtaining ethical clearance.

METHODOLOGY:

The study subjects were first clinically evaluated based on age, sex, morphology, association with other corynebacterial infections, other dermatological lesions and then blood sugar, thyroid levels done. Specific investigations like gram stain ,Wood's lamp ,skin biopsy and culture being done. Then 25 patients randomly allocated into two groups. Group A patients were treated with 2% clotrimazole cream and group B were treated with 2% fusidic acid cream applied twice daily. The patients were followed up for 2 weeks. The schedule of patient visit is as follows Visit 1 for initial or baseline assessment and follow-up at 7th & 14th day.

STATISTICAL ANALYSIS:

The data collected were analyzed using Student t test (two tailed,independent) to find the significance of study parameters on continuous scale between two groups. Chi-square/ Fisher Exact test was used to find the significance of study parameters on categorical scale between two or more groups.

RESULTS :

Erythrasma was found to be common in 58 % female patients and 50% were in middle age group. Morphologically reddish brown lesions were found in 88 % patients with involvement of groin mostly . 10 cases were associated with keratolysis punctata and 8 cases with trichomycosis axillaris . Diabetes mellitus, hypothyroidism and obesity associated. 2% fusidic acid cream was found to be more effective than 2% clotrimazole cream in reduction of colour intensity, demarcation .scaling and Wood's lamp reflection score. Side effects were not seen in both groups.

CONCLUSIONS:

Erythrasma was common in middle aged females with reddish brown lesions in groin. It was found to be associated with keratolysis punctata, trichomycosis axillaris, acanthosis nigricans,acrochordons and systemic diseases like diabetes mellitus , hypothyroidism. 2% fusidic acid cream was found to be effective bactericidal than 2% clotrimazole cream in erythrasma.

KEY WORDS:

Erythrasma , 2% clotrimazole cream, 2% fusidic acid cream , efficacy, keratolysis punctata, trichomycosis axillaris, diabetes mellitus ,obesity , Wood's lamp

INTRODUCTION

The normal human skin surface and its follicles is colonized by huge numbers of bacteria that live harmlessly as commensals . At times the overgrowth of some of these resident organisms may cause minor disease of skin or its appendages. If the immune status of the subject is impaired or the skin is damaged, bacteria usually regarded as nonpathogenic on body surface will assume the role of opportunist pathogens.

Erythrasma is a chronic superficial bacterial infection of the skin widely prevalent all over the world. The causative agent is a gram positive aerobic diphtheroid called *Corynebacterium minutissimum*. Studies carried out by scientists regarding its microbiology, pathogenicity, biochemical characters and treatment has expanded our knowledge about the condition. These organisms normally contribute to cutaneous ecosystem. But when local or systemic devitalizing factors are favourable , they behave as pathogens.

Recently various studies has been conducted for therapeutic trials in erythrasma using topical imidazole group of antifungals or fusidic acid and oral macrolides .

REVIEW OF LITERATURE

HISTORICAL ASPECTS

A German scientist Burchardt in 1859, was the first to describe the disease and suggested that the delicate filaments and granules found in the scales were of fungal origin and were the cause of the disease ^[1].

The term 'erythrasma' was coined in 1862 by Von Baren Sprung, Burchardt's teacher. He named the causative organism as *Microsporum minutissimum*.

Most of subsequent workers like Koebner 1884; Balzer and Dubrevilh 1883; Unna 1896 had no doubt that erythrasma was a separate entity. Some workers including Weyl (1884) considered that various transitional forms existed between erythrasma and pityriasis versicolour. Gougerot (1936) was the one to recognise disseminated and subacute forms of erythrasma and pointed out that the condition can be complicated by eczematization or can be associated with bacterial or fungal infections. Koebner in 1884 was the first person to reproduce disease by applying the scales infected with erythrasma to the skin of one of his pupils ^[2].

The numerous names appeared in the literature for the causative organism of erythrasma includes *Microsporum minutissimum*, *Nocardia minutissimum* and *Sporotrichum minutissimum* ^[3].

Poehlmann (1928) considered local factors such as site, humidity, body secretions, individual predisposition, sweating, a delicate integument and systemic illness like diabetes mellitus for the causation of erythrasma.

Robean and Guerra (1936) gave an account of 16 patients with the condition involving the toe-webs and few of them had associated fungal infection.

Nikolowski and Stable (1949) reported an unusual form of erythrasma involving forearms . The generalised form was reported by Goncalves and Mangeon (1960) which is characterised by well defined scaly lamellated plaques in the trunks and limbs.

Lagana (1960) was the first to suggest the bacterial cause for erythrasma . Sarkany, Taplin and Blank (1961) isolated a diphtheroid which they named *Corynebacterium minutissimum* from the lesions of erythrasma and thus gave way for a new outlook on the condition for subsequent scientists to carry out their work ^[4]. Now various studies are being carried out relating erythrasma to obesity, diabetes mellitus and its association with other fungal conditions like pityriasis versicolour and dermatophytosis.

EPIDEMIOLOGY OF ERYTHRASMA

The incidence of erythrasma is reported to be around 4.5%. This infection is observed all over the world; the widespread form is found more frequently in the subtropical and tropical areas. Mild forms of erythrasma of axilla, groins and toe-webs are relatively common in temperate climates; the less common generalised form is predominantly seen in obese subjects particularly in middle aged Negro women.

Incidence is higher in communities like the armed forces and various institutions. In some institutions, the infection appears to be endemic and the incidence among the patients remaining relatively constant over a period of years. Sarkany, Taplin and Blank in 1962 found that the incidence is higher in tropical climates and generalized type is frequently common^[5]. The incidence usually increases with age and a case has been recorded in one year old child which was studied by Laube S (2004) ^[6].

Eventhough both sexes are equally affected by erythrasma, the crural form of erythrasma is more common in men. A study conducted in the year 2008 found out that interdigital erythrasma was more common in women ^[7].

Erythrasma is not significantly contagious. Holdiness (2003) found out that factors such as warm climate, poor hygiene, obesity, hyperhidrosis, advanced age and diabetes mellitus play a role in the occurrence of the disease ^[8].

Bowyer A (1971) showed that erythrasma could be associated with pruritus ani^[9]. A study reported that 11% patients with mental abnormalities had involvement of perianal areas.

The association of erythrasma with dermatophytosis of groin was reported by Schlappner OL, Rosenblum GA in 1979 ^[10]. When lesions were seen in groin and axillae, it was associated with pityriasis versicolour ^[11].

The incidence and severity of erythrasma is apparently greater amongst diabetics . Somerville and Lancaster in 1973 found that carriage of fluorescent diphtheroid was greater even in milder forms of diabetics ^[12]. It is possible that diabetics are as susceptible to erythrasma like candidiasis and this is perhaps related to the high levels of free glucose in the skin as shown in a review article by Haroon TS (1974) ^[13]. Montes LF and Dobson H et al also studied the association of diabetes mellitus and erythrasma in 1969 ^[14]. Obesity is a predisposing factor for the development of erythrasma was reported by Schein-feld NS (2004). The occurrence of erythrasma is not affected by use of deodorants ^[15].

NORMAL CUTANEOUS FLORA AND DIPHTHEROIDS

For a better understanding of the disease, it is important to mention a few words about the normal flora of skin.

Skin bacteria are of 2 types transients and residents. Transients are most abundantly present on exposed skin and few numbers are seen on clean unexposed skin. The resident flora is a relatively stable both in composition and size.

Gram positive cocci like *Staphylococcus* species and *Micrococcus* species, Gram positive rods like the coryneform mainly *Corynebacterium* spp. and *Brevibacterium* species constitute aerobic resident flora. The only significant gram negative residents are *Acinetobacter* species which was previously known as *Mima* and *Herellea*. The coryneform (or diphtheroid) organisms are mostly Gram positive nonsporing aerobic pleomorphic rods.

The coryneform bacteria are difficult to get separated by conventional taxonomic methods and chemotaxonomic methods. The aerobic coryneforms are divided into four *Corynebacterium* species complexes -*C. xerosis*, *C. minutissimum*, *C. bovis* and *C. hofmani* with *Brevibacterium* and *Propionibacterium* spp. making up a total of six groups by recently proposed scheme ^[16].

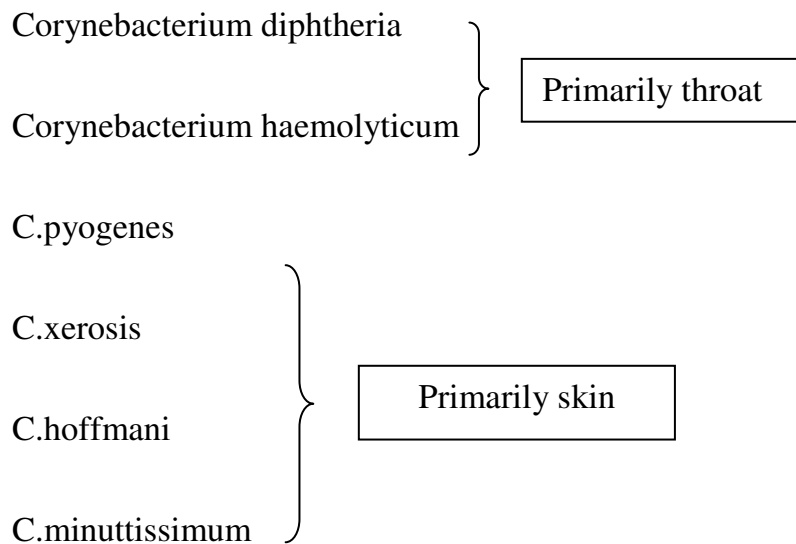
Cutaneous diphtheroids initially were assigned to different groups based on their oxygen requirements. The anaerobic under the term *Propionibacterium acnes* and aerobic diphtheroids are classified according to their origin, tyrosine clearance,

obligate lipophilicity and nitrate reduction. *P.acnes* are mainly associated with follicles over face and upper trunk as they have large pilosebaceous glands ^[16]. It has a role in pathogenesis of acne lesions .

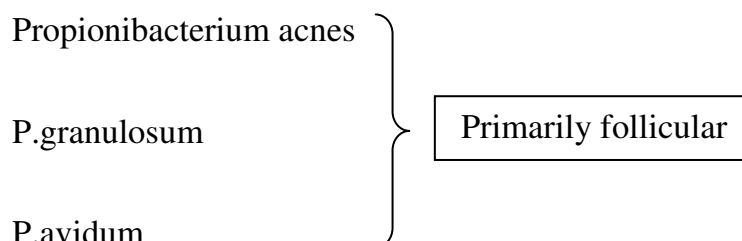
CORYNEFORM BACTERIA

They are human commensals or pathogens

Aerobic



Anerobic



Pathogens which sometimes infect humans

Listeria monocytogenes

Erysipelothrix rhusiopathiae

In adult life, aerobic diphtheroids are commonly found in large numbers on the skin. Two characteristic features of these aerobic diphtheroids are porphyrin production and lipophilia. Sebum is an important source of metabolites for both the anaerobic and aerobic diphtheroids. All lipid dependent strains hydrolyse palmitate which is the most common fatty acid formed in human surface lipids.

Porphyrin production could be demonstrated by examining under UV light which shows typical coral red fluorescence in the cultures grown on suitable media. Sarkany, Taplin & Blank detected that porphyrin production by the diphtheroid was responsible for erythrasma in 1961^[17]. This characteristic is more prevalent amongst corynebacteria than expected. In addition to *C. minutissimum*, *C. bovis*, *C. xerosis*, primarily follicular *C. ulcerans* and *C. renale* also show fluorescence. *C. diphtheriae* is known to produce coproporphyrin III under conditions of iron deficiency and the red fluorescence of the comedones of face has been shown to be due to the production of protoporphyrin IX and coproporphyrin III by *P. acnes*.

In 1973, Somerville used nine simple tests (lipophilia, glucose fermentation, nitrate reduction) to arrange the aerobic cutaneous diphtheroids into 15 groups in which seven were porphyrin producers and eight were non-porphyrin producers^[12].

Montes and his colleagues demonstrated an apparent bacteriophage cycle in diphtheroids on human skin using an electron microscope. Phages have been isolated from various species of corynebacteria other than *C. diphtheriae*.

In most people the aerobic diphtheroids can be isolated from the skin in virtually all parts of the body. They are particularly common in groin, axilla and toe webs.

Age has an important role in determining the occurrence of the infection. In newborn period, relatively few organisms are seen and within few hours there is an increase in number. Incidence increases in childhood with highest in young adults. It has been suggested that increase in the amount of sebum secreted on to the skin at puberty favours the survival and growth of these organisms as they are lipolytic and some lipophilic. In the axilla the micrococci with diphtheroids contribute to the development of axillary odour.

The role of diphtheroids as normal flora is high. They cause erythrasma, keratolysis punctata, trichomycosis axillaris and acne only in few people.

MICROBIOLOGY OF CORYNEBACTERIUM MINUTISSIMUM

C. minutissimum which is an aerobic diphtheroid has common morphologic features of diphtheroids. On staining with Gram stain, the isolates from the skin lesions of erythrasma show rod like organisms, coccoid forms and filaments. The filaments measure about 4µ to 10µ by 1µ and are tortuous. The longer filaments have beaded or segmented appearance. The bacillary forms are about 1µ-3µ in length and 0.5µ in diameter. Some reveal subterminal granules.

The shorter forms are more profuse in the erythrasma lesions of toes, however chains of bacilli and filamentous forms are also found^[1]. The lesions often contain higher proportion of filaments and few shorter bacillary forms.

Under electron microscope ^[18], most of the bacteria will be seen at the level of stratum corneum. They are proliferating over the skin surface between cornified cells. They penetrate these cells from the intercellular space, directly from the skin surface or intracellularly within the keratinised cells.

Most of the organisms within the skin surface have homogenous fine structures. But in the stratum corneum pleomorphism is observed. Also multiplying organisms are more common on the surface than within the stratum corneum.

The stratum corneum is hyperkeratotic with superficial layers being widely separated and cell boundaries getting disrupted at the sites of penetration of organisms. Cytoplasmic areas of keratinocytes show decreased electronic density which is observed mainly around the intracellular bacteria probably suggesting a keratolytic process.

Electron micrographs of the full stratum corneum thickness showed that the bacteria in erythrasma will penetrate as deeply as one-half of the thickness of that layers. Bacteriophages can apparently exist within the bacterial cell ^[19].

Skin surface biopsy technique was used by R.Marks and N.D.Ramnarain (1972) to study erythrasma patients ^[3]. The skin surface biopsies were subjected to scanning electron microscope studies and enzyme histochemical reactions. Skin biopsies from the affected sites when stained with Periodic Acid Schiff (PAS) reagent or Gram stain demonstrated the presence of numerous fusiform microorganisms which are arranged in clusters, singly or chains and scattered over

various areas .The chains were usually comprised of three, four or occasionally more bacterial cells. The microorganisms were approximately three to four times longer than broader.

There was noticeable diffuse staining of the sites containing the microorganisms which was visible macroscopically with PAS stain. There was not any particular accentuation around hair follicles or sweat gland openings.

Corynebacterium minutissimum possess a wide range of enzyme activities as shown by enzyme histochemical methods. Mitochondrial enzyme activities especially Nicotinamide Adenine Dinucleotide diaphorase and lactic dehydrogenase activities were particularly strong. The reaction products from the tests performed were not diffusely distributed within the individual bacterial cells but appeared as well defined foci of aggregations within each cell.

Single rod shaped and oval structures and chains were seen lying embedded in the surface of the individual cornified cells with the scanning electron microscope. The surface of the cells were regularly smooth. The chain of bacterial cells would frequently seen to be penetrating the cornified cells. Several scales openings at the site of penetration were two or three times larger than the diameter of the microorganisms.

The cells in the stratum corneum which are involved had an irregular ridge pattern mainly composed of low broken undulating ridges which were sometimes branched. The surrounding uninvolved cells usually possessed prominent villi that

resembled the surface structure of the scale in psoriasis and other parakeratotic disorders (Dawber, Marks and Swift, 1972).

This skin surface biopsy study showed that there was a remarkable difference between the numbers of bacteria seen in stained preparations with light microscope and scanning electron microscope. This is probably a reflection of the fact that the surface showed by scanning microscope is five or six cell layers down into stratum corneum, while the light microscope shows the whole thickness of the specimen removed.

Montes, Black and McBride (1967) demonstrated that the great majority of microorganisms of erythrasma does not invade beyond the superficial part of the stratum corneum by conventional electron microscope ^[20].

The surfaces of the horn cells penetrated by the micro organisms possessed a disorganized ridge pattern that suggests a possibility of disruption of the tonofilament desmosome complexes. At the site of penetration, the opening was wider than the micro organisms. This suggests that penetration was usually accomplished by a chemical dissolution rather than physical pressure.

Montes et al. (1967) noted there was disorganization of keratin fibrils in horn cells invaded by *C. minutissimum*. The enzyme reaction products showed aggregations in well defined areas confirming a complex subcellular arrangement akin to mammalian cells. Also a similar arrangement has been noted with enzyme reactions in the dermatophyte fungi (Meinhof, 1968).

The smooth exterior of the organism observed by scanning electron microscope showed only a slight constriction at the site of the junctions between microorganisms in chains . The PAS reactivity of the microorganisms reflects the secretion of mucopolysaccharide sheath by the organism in some situations.

Somerville (1972) discussed the microbiology of cutaneous diphtheroids and stated that the diphtheroids responsible for trichomycosis axillaris produced secretions that stick them together and to the hair along with destruction of the hair keratin. A similar material might be produced by *C.minutissimum* ^[12].

Tissue Culture Medium 199 for growing the organisms under specific conditions was devised by Sarkany, Taplin and Blank ^[4]. This medium consist of 78% tissue culture medium without bicarbonate, 20% fetal bovine serum and 2% agar. The prepared medium being autoclaved for 10 mts at 15 lbs pressure per square inch. Plates were poured by decanting the hot liquid from the coagulated proteins which are discarded. On inoculation at 38° C, the fluorescent scales of erythrasma lesions shows small shiny, round, translucent, colourless, slightly elevated convex colonies within 24-48 hours. There is no pigment production in visible light, although a red fluorescence diffusing into the surrounding medium can be observed under Wood's light. Some batches of fetal bovine serum shows an inhibitory effect on the growth of the organisms . Autoclaving the medium or using a dialysate of fetal bovine serum will promote the growth and fluorescence. Inhibition of growth can also take place, when autoclaved medium 199 is used with human or horse serum.

Certain batches of Tissue Culture Medium 199 are marketed with the added antibiotics such as penicillin or streptomycin. Such media are unsuitable as they suppress the growth of the organisms. A pink fluorescence in and around the colonies can be seen on sheep blood agar, chocolate agar and yeast extract casein agar, but the fluorescence assumes striking proportions only on the tissue culture medium. Subculture of the organisms can be done on a large number of bacteriological media. They can also thrive on the chorioallantoic membrane of ten day old embryonated eggs at 38°C.

Gram stain of a smear from a colony shows Gram positive rods but appears pleomorphic in older cultures. These organisms are non-motile, aerobic or microaerophilic. They are catalase positive, indole negative, contain metachromatic granules and do not show hemolysis. They ferment fructose, mannose, maltose and in some strains sucrose. Dark field microscopy shows typical bacilli with a marked thick outer wall and well rounded ends. In vitro sensitivity tests carried out on solid and liquid media showed maximal sensitivity to erythromycin.

Sarkany and his colleagues used pure culture to stripped or scarified areas of skin of forearms and kept them occluded for 72 hrs. Scaling and fluorescence were seen in three out of five inoculations. These were of relatively short duration and did not develop into permanent erythrasma. Fluorescent cultures also were reobtained from these experimentally induced lesions. Hence Sarkany et al. showed that this organism fulfill the criteria of Koch's postulates ^[1].

The grouping scheme proposed by Somerville shows that any of the seven groups of fluorescent diphtheroid might be isolated from the lesions of erythrasma . Using this grouping scheme Somerville and her colleagues found that in their community, one particular group which represent endemic strain was more commonly associated with erythrasma than with healthy skin . Group 2 was the initial isolate described by Sarkany, Taplin and Blank and used as type strain in the National collection of type culture ^[4].

It is clear that fluorescent diphtheroids associated with erythrasma are members of normal skin flora which eventually produce the characteristic fluorescing lesions of erythrasma and multiply under certain conditions like chafing , maceration in axilla and groins to become predominant members of the skin flora . Non fluorescent diphtheroids also appear in great numbers in these lesions rather than on healthy, non scaling, non fluorescing areas. So these conditions favour the multiplication of all type of skin diphtheroids.

PATHOGENESIS

The skin along with mucous membrane forms the first line of defense against infection. Both keratinization and dryness limit the proliferation of microorganisms which is supported by low pH of skin surface ^[21]. These characteristics limit the colonization of commensal organisms. Microorganisms causing any skin infections need to overcome the above defense mechanisms. These organisms enter through an intact epidermis either by lysing the keratinocytes or mechanically destroying it. Some organisms look continuously for an opportunity to get under the epithelium through a break in epidermis which is usually traumatic.

The stratum corneum consists of mainly keratin mixed with lipids secreted by different skin appendages. These lipids are used as substrate for metabolism by the organisms that parasitise on the skin which are mostly commensals^[22]. Often their presence goes unnoticed until there is enough substrate available for them to outgrow in numbers evoking an inflammatory response of underlying tissue. This results in itching with or without erythema. Erythrasma is one such disease that originate almost exclusively from skin folds where the concentration of secretory glands are highest ^[23].

Thus the *Corynebacterium minutissimum* which is a commensal being lipophilic produces lesions predominantly involving flexures and outgrows in number due to excessive sweating and maceration.

Corynebacterium species other than *C.diphtheriae* are known to produce severe and life threatening infection . There have been no previous reports of deep tissue invasion by *Corynebacterium minutissimum* except one study by Stephen A Berger et al. which reports recurrent breast abscesses caused by *Corynebacterium minutissimum* in one of his patients ^[24]. There was no evidence suggestive of erythrasma in the patient but had skin disruptions. Local trauma might have served as the portal of entry leading to invasive infections.

CLINICAL FEATURES

The common sites of involvement are groin, upper thigh, scrotum, axillae, pubis, inguinal folds, inframammary areas and toe webs. In toe webs, infection is chronic being most commonly between 4th & 5th toe followed by 3rd and 4th toes ^[25]. There may be scaling, maceration and fissuring.

Cabo H et al (1983) have described a case of generalised erythrasma in a patient with Type II diabetes mellitus ^[26]. Well defined scaly, lamellar plaques in larger areas of trunk, proximal parts of limbs and breast folds may occur in generalised forms. Discoid form ^[27] of erythrasma with circular scaling patches are easily confused with pityriasis versicolour, pityriasis rotunda and psoriasis. This form being also called as tropical erythrasma ^[28]. Tschen JA and Ramsdell WM in 1983 presented a case of disciform erythrasma . It was clinically characterised by surface with atrophy and diagnosis was made with help of Wood's light examination and Gram stain.

The classic form appears as punctate, well circumscribed, maculopapular lesions with furfuraceous or greasy scales. Older lesions have fine scaling with serpiginous advancing ends. The colour of lesion depends upon duration and underlying skin pigmentation. It is pink in colour initially later changes to brown without central clearing. Occasionally vesiculation of lesion was reported by Grigoria and J.Delacretaz in interdigitopantar type of erythrasma ^[29]. Pruritus is followed by vesiculation in the lesions. The lesions are initially vesicles with erythema followed by large bullae which contains yellow fluid which becomes opalescent later. Rarely lesions may become eczematous. Many of the lesions were asymptomatic and patients seek medical attention for cosmetic disability. Occasionally these lesions are very itchy. Recurrence and chronicity are noted in many cases. A.Bowyer & McColl described association of erythrasma with pruritus ani ^[9]. The longstanding pruritus was cured with erythromycin.

Negroni P ^[30] in 1976 reported that toe nails may be involved in erythrasma with subungual hyperkeratosis and onycholysis. Shelley WB and Shelley ED (1982) studied the corynebacterial triad consisting of coexistent erythrasma, keratolysis punctuata and trichomycosis axillaris. They showed that trichomycosis axillaris caused by *Corynebacterium tenuis* and keratolysis punctata caused by *Corynebacterium taplin* were associated with erythrasma in few patients ^[31].

Few systemic infections can also occur due to *Corynebacterium minutissimum*. *Corynebacterium minutissimum* bacteremia in a patient with a chronic myeloid leukemia in blast crisis was reported by Guarderas J and A.Karnad

(1986)^[32]. Brian H.J. and Brucker A.J reported embolic retinopathy due to *C.minutissimum* endocarditis in 1985^[33].

Alfred Gorea and Stephen A Berger in 1984 reported recurrent breast abscesses caused by *C.minutissimum*. The systemic infections that can occur due to *C.minutissimum* are

- i) infective endocarditis in valvular heart disease patients
- ii) septicemia in neutropenic patients
- iii) post surgical wound infections
- iv) recurrent abscesses.

INVESTIGATIONS

i) Wood's lamp examination:

Wood's lamp is a high pressure mercury lamp with a special filter that allows the emission of a largely monochromatic UV light with a wavelength of 365 nm^[27]. It is especially useful in the diagnosis of certain bacterial and fungal disease and in the assessment of pigmentary disorders.

For examination, the room should be completely darkened with the patient totally undressed. Lesions caused by *Microsporum canis*, *M.audouinii* and *M.ferrugineum* are identified by their blue-green fluorescence. Pityriasis versicolour lesion shows a golden yellow fluorescence. *Pseudomonas aeruginosa* lesions give rise to a blue colour.

Depigmentation or hypopigmentation are more easily detected with the aid of Wood's lamp. In patients suspected of having porphyria, urine, stool and red blood cells are screened with Wood's lamp provoking a characteristic orange-red fluorescence.

In erythrasma the suspected lesions when examined with Wood's light show coral red fluorescence due to porphyrin production by *Corynebacterium minutissimum*.

An extensive work on fluorescence with Wood's light was done by Wigger Alberti N and Elsner P in 1997 and they showed that if the lesions are washed with antibiotic soaps before Wood's lamp examination, fluorescence may be transiently absent^[34]. Sometimes fluorescence may persist even after treatment of erythrasma. A case of non fluorescent erythrasma of the vulva was described by Mattox TF and Rutgers J (1993) which was diagnosed by Gram stain and culture^[35].

Other lesions which give pink fluorescence under Wood's lamp examination are

- i. Normal tongue
- ii. Necrotic tumors
- iii. Openings of follicles of face and upper trunk
- iv. Acanthosis nigricans of groin and axilla

2. Direct Examination:

a) Gram stain:

The scales from the lesion are scraped and fixed to the slide using egg albumin. Alternatively Padilha (1996) described a single method to stain *C. minutissimum* and *Malassezia furfur* in scales collected on scotch tape with lactophenol cotton blue ^[36]. On staining Gram positive filamentous and coccoid forms were seen.

b) 10% KOH preparation:

10% KOH solution is added to the scrapings from the lesion and examined under light microscope. Chains of rods are seen.

c) Culture

Culture is difficult but rarely necessary and may be accomplished with a special medium the ideal one being Tissue culture medium 199. Simple mediums for pigment production by *Erythrasma diptheroid* were described by Stephen N Cohen and Dorothy Nicholai in 1969 ^[37].

The scales of *Erythrasma* lesion on inoculation at 38°C for 24-48 hours shows smooth small shiny translucent convex colonies. These colonies can fluoresce for upto 4 days under Wood's lamp. Gram stain of smear from a colony shows Gram positive rods in freshly prepared cultures, later become pleomorphic in older cultures.

d) Skin biopsy:

Biopsy of erythrasma lesion usually appears normal. It is described as one of the examples of invisible dermatoses. Small coccobacilli might be seen in the superficial layers of stratum corneum ^[38]. Though difficult to visualise under Hematoxylin and Eosin stain, special stains like Gomori's Methanamine silver stain and Periodic Acid Schiff will reveal these coccobacilli.

e) Others

Investigations for underlying factors such as diabetes mellitus, obesity and hypothyroidism should be carried out.

DIFFERENTIAL DIAGNOSIS

1. Pityriasis versicolor – chronic type

The primary lesion is a sharply demarcated macule which is characterised essentially by fine branny scaling. Typically the eruption shows large confluent areas, scattered oval patches and outlying macules. Most commonly upper trunk which is rich in seberrheic secretion gets affected but can spread to upper arms, axillae , groins and abdomen ^[40]. The scaly lesions under Wood's lamp may show pale yellow fluorescence. In these cases, axillary vault will not be involved.

2. Bacterial Intertrigo

It is an inflammatory condition of opposing skin surfaces characterized by erythema , oozing , maceration and crusting ^[39]. Vesicles and pustules may herald the infection. Triggering factors include perspiration, friction, maceration or irritation from stool, urine or topical agents. KOH examination, Gram stain and culture help to identify the organism.

3. Candidal intertrigo

Most cases of cutaneous candidosis occur in skin folds which are occluded by clothing or shoes producing abnormally moist conditions. Clinically presents with erythema, cracking and maceration. Lesions have an irregular margin with surrounding satellite papules and pustules. 10% KOH preparation reveals yeast and pseudohyphae.

4. Tinea cruris

It manifests as large plaques of erythema with central clearing centered on the inguinal creases and extend distally down the medial aspect of the thighs with scaling at the periphery. 10% KOH examination reveals septate branching hyphae with arthrospores. Woods lamp examination is negative unlike erythrasma.

5. Inverse pattern psoriasis

Psoriasis is a chronic, relapsing inflammatory keratinization skin disorder with a strong genetic basis characterized by circular to oval erythematous plaques over extensor body surface and the scalp. Inverse psoriasis is a variant of psoriasis that spares the typical extensor surfaces and affects intertriginous areas with minimal scaling. Skin biopsy confirms the diagnosis.

6. Flexural seborrheic dermatitis

Seborrheic dermatitis is a papulosquamous inflammatory disorder occurring on sebum rich areas of scalp, face, upper trunk characterized by greasy scaling over erythematous skin. The flexural variants are non scaly lesions occurring in axillae, perineum or anogenital crease, inframammary and inguinal folds.

7. Contact Dermatitis

Allergic and irritant contact dermatitis may mimic erythrasma. Irritant contact dermatitis manifests as erythema and hyperkeratosis but allergic contact dermatitis presents as pruritic papules and vesicles on an erythematous base.

Bacterial culture and 10% KOH examination are done. Patch test helps to diagnose contact allergens.

8. Acanthosis nigricans

It is characterised by symmetrical hyperpigmented velvety plaques most commonly on the intertriginous areas of the neck, axillae and groin. Skin biopsy is the useful aid in the diagnosis.

9. Pityriasis rotunda

A case of pityriasis rotunda mimicking erythrasma was reported by Gupta S (2001) ^[41]. It is a rare disease characterized by perfectly round to oval sharply defined, hypo or hyperpigmented patches over trunk and extremities with mild scaling.

TREATMENT

The organism involved in this disease are sensitive to many antibiotics. Erythromycin was first suggested by Sarkany et al for treatment of erythrasma. Erythrasma responds to keratolytic preparations and antimicrobials, but toe web infections are difficult to cure ^[42].

Erythrasma responds well to topical agents like 2% sodium fusidate, Whitfield's's ointment, tolnaftate, 1 to 2% clotrimazole, miconazole , 10 - 20% aluminium chloride and 2% clindamycin hydrochloride.

Clinical clearance and disappearance of red fluorescence after 2- 3 weeks in eight patients treated with tolnaftate with no relapses was achieved by Ayres and Mehan (1968) . In 1970 Macmillan and Sarkany proved that sodium fusidate to be effective particularly in the removal of fluorescent diphtheroids but it was not more effective than Whitfield's ointment in producing resolution of clinical lesions. Seville and Somerville found that Whitfield's ointment was more or less equally effective. Gaylon and Lonnor B.C in 1973 showed that Whitfield's's ointment and clotrimazole were shown to be equally effective .

Topical clotrimazole and tolnaftate lead to resolution of lesions mostly associated with dermatophyte infections. Also topical nadifloxacin and clarithromycin can be used. Topical erythromycin has not been consistently effective.

Koorshad studied adult male population and found out antibacterial soap was effective in the prophylaxis and control of erythrasma of toe webs. The vigorous use of any soap under trial conditions reduced the incidence of erythrasma, but the antibacterial soaps are more effective and better in reducing the amount of scaling was demonstrated by Somerville, Seville and Noble (1970). Benzoyl peroxide or povidone iodine soaps when showering and powders after drying are also effective.

Systemic erythromycin is consistently effective in doses of 250mg qid for 5 days by some and for 10 - 14 days by others. Holdiness MR (2002) showed that in patients with involvement of axilla and groin, systemic erythromycin when compared with tetracycline has greater efficacy^[43]. Griseofulvin and penicillin are ineffective. Erythrasma can be treated with 1gm single doses of clarithromycin was demonstrated by Wharton JR and Wilson PL (1998)^[44].

Photodynamic therapy using red light (broadband, peak at 635 nm) has been reported to clear erythrasma in 23% of 13 patients and improved erythrasma in the remaining patients^[59].

In a recent susceptibility study of 40 patients, several antibiotics were tested including penicillin G, ampicillin, cefaclor, amoxicillin-clavulanate, ampicillin-sulbactam, tetracycline, erythromycin, ofloxacin, fusidic acid, levofloxacin and azithromycin. The study revealed statistically significant resistance to erythromycin, azithromycin, penicillin and ampicillin. Significant susceptibility was statistically found to amoxicillin-clavulanate, cefaclor and fusidic acid^[60].

In a large double-blind, placebo-controlled, randomized trial, 151 patients older than 18 years were randomized into 5 groups and were given either erythromycin, single-dose clarithromycin, topical fusidic acid, placebo cream or placebo tablets. Fusidic acid cream was significantly more effective than other therapies. Additionally, the group who received clarithromycin did better at 48 hours than did the group that received erythromycin. However, there was no statistical difference on day 7 and day 14 ^[61].

Because culture and antibiogram are not performed routinely in daily clinical practice, the recommended initial topical treatment is fusidic acid cream. If this drug is not available, then topical erythromycin solution may be an alternative. In cases of topical treatment failure, erythromycin, single-dose clarithromycin, or amoxicillin-clavulanate should be chosen for the systemic treatment ^[60].

Prognosis:

Excellent, however recurs if predisposing factors are not eliminated.

Prevention:

- Bathe or shower often
- Keeping skin dry
- Wear clean clothes that absorb moisture
- Avoid very hot or damp conditions
- Maintain a healthy body weight

CLOTRIMAZOLE

It is an azole antifungal which belong to imidazole group.

Mechanism of action

Clotrimazole interacts with 14- α demethylase, a cytochrome P-450 enzyme that converts lanosterol to ergosterol, an essential component of the membrane of the yeast ^[45] and inhibits ergosterol synthesis, resulting in increased cellular permeability. It may also inhibit endogenous respiration, interact with membrane phospholipids, inhibit the transformation of yeasts to mycelial forms and the uptake of purine, impair triglyceride and/or phospholipid biosynthesis, and inhibit the movement of calcium and potassium ions across the cell membrane by blocking the ion transport pathway known as the Gardos channel.

Absorption

Absorption of clotrimazole is less than 0.5% after application to the intact skin; from the vagina, it is 3% to 10%. The small amount absorbed is metabolized in the liver and excreted in bile ^[45].

Drug interactions

There are no known significant drug interactions with topical clotrimazole. However, with oral (troche) clotrimazole, there are multiple interactions as the medication is a CYP450 enzyme inhibitor, primarily CYP3A4. Thus, any medication that is metabolized by the CYP3A4 enzyme will potentially have elevated levels when oral clotrimazole is used ^[46].

Side effects

In a small fraction of recipients, clotrimazole on the skin may cause stinging, erythema, edema, vesication, desquamation, pruritus and urticaria ^[45]. When it is applied to the vagina, about 1.6% of recipients complain of a mild burning sensation and rarely of lower abdominal cramps, a slight increase in urinary frequency, or skin rash. Occasionally, the sexual partner may experience penile or urethral irritation. By the oral route, clotrimazole can cause gastrointestinal irritation. In patients using troches, the incidence of this side effect is about 5%.

Antimicrobial activity

Clotrimazole is active against dermatophytes, molds, fungi of the genus *Candida* and *Malassezia furfur*. This drug is also active against *Corynebacterium minutissimum*, *Streptococcus* spp., *Staphylococcus* spp. and *Trichomonas vaginalis*^[47].

Trials in erythrasma

A double-blind trial was used to compare the efficacy and acceptability of topical treatment with clotrimazole cream or Whitfield's's ointment for ringworm, pityriasis versicolour, and erythrasma infections and that of clotrimazole cream or Nystatin ointment for *Candida* infections. Clotrimazole was found to be as effective and acceptable as Whitfield's's ointment and Nystatin ointment.

A clinical double-blind trial of topical miconazole and clotrimazole creams was carried out against superficial fungal infections of the skin. The trial showed both compounds to be very effective against dermatophytes, pityriasis versicolour, Candida and erythrasma infections. Patient acceptability was equally good for both compounds ^[64] .

FUSIDIC ACID

Fusidic acid is derived from the fungus *Fusidium coccineum* and was developed by Leo Laboratories in Copenhagen, with the most active derivative, the sodium salt (sodium fusidate), released for clinical use in the early 1960s ^[48].

Mode of Action

A crucial stage in bacterial protein biosynthesis is the elongation phase, in which the nascent polypeptide grows as the ribosome moves along the mRNA in a stepwise fashion. Two elongation factors, EF-Tu and EF-G, are intimately involved in this process, with EF-G particularly associated with the translocation step in which the mRNA is advanced along the ribosome by 1 codon to allow the next round of polypeptide elongation to begin ^[49]. Fusidic acid blocks bacterial protein synthesis by binding to EF-G on the ribosome, thereby preventing release of the EF-G—guanosine diphosphate complex and effectively stalling bacterial protein synthesis by inhibiting the next stage in translation ^[49–51]. The action of fusidic acid is mainly bacteriostatic but, at high concentrations, may be bactericidal. The gene encoding EF-G is *fus A*, which is chromosomally located.

Antimicrobial activity

Fusidic acid has good *in vitro* activity against staphylococci, including both methicillin sensitive and resistant strains. It also has useful activity against *Neisseria* spp, *Bordetella pertussis*, *Corynebacterium* spp, Gram positive anaerobes

such as *Clostridium difficile* and *C.perfringens*, *Peptostreptococcus* spp and *Propionibacterium acnes* ⁵².

Pharmacokinetics

Penetration of fusidic acid applied topically to the skin is minimal with studies showing absorption of 2% or less ^[53].

Distribution

Fusidic acid has modest penetration into bone (16 – 24%) and synovial fluid (28-88%) and achieves levels in pus that are marginally below those in serum. Skin exudate and burn studies show good C_{max} values and high fluid/serum ratios ^[54].

Metabolism

Hepatic metabolism with biliary excretion is the most likely route of elimination, although renal elimination of hepatic conjugates or metabolites has not been specifically reported. Examination of biliary metabolites of fusidic acid shows that the main metabolites are a glucuronide conjugate and a dicarboxylic derivative, accounting respectively for 15% and 10% of the drug in bile. A variety of minor metabolites are produced ^[54].

Topical Preparations

There are three preparations- 2% fusidic acid cream, 2% fusidic acid ointment and 2% fusidic acid gel all for use on skin surfaces twice daily.

Skin Reactions

Contact dermatitis occurs in some patients after topical use but is uncommon^[55]. Often it has been associated with use in patients with stasis ulcers.

Drug interactions

Hepatic cytochrome P450 enzyme interactions have been described for fusidic acid. Levomethadone metabolism is increased during prolonged fusidic acid therapy due to induction of cytochrome P450 isoenzymes^[56].

In erythrasma

Sodium fusidate ointment has been used in the treatment of erythrasma in a mental hospital. In comparison with a benzoic acid (Whitfield's) ointment it proved as effective in clearing fluorescent lesions (90%,cure) and more effective in clearing the associated *Corynebacterium minutissimum*. It was, however, less effective in removing scaling^[62].

In a Danish multi-practice study the efficacy of erythromycin tablets 500 mgs , fusidic acid cream and placebo was compared in 86 patients (71 men and 15 women) with erythrasma. The patients were treated 'double-blind' for 14 days with either active tablets + placebo cream, placebo tablets + active cream or placebo tablets + placebo cream. The signs of erythrasma, i.e. colour intensity, demarcation and scaling of the affected area, as well as degree of fluorescence under Wood's light, were recorded before treatment, after one and two weeks, and at follow-up four weeks later. Cure/improvement was obtained in 77% of the cases in the erythromycin group, 87% in the fusidic acid group and 42% in the placebo group. There was no difference between the active preparations^[63].

AIMS OF THE STUDY

1. To study the age and sex distribution of the patient.
2. To study the clinical profile of erythrasma.
3. To study the predisposing conditions.
4. To study the association of other corynebacterial skin infections.
5. To compare the efficacy of topical 2% clotrimazole cream vs 2% fusidic acid cream in the treatment of erythrasma.

MATERIALS AND METHODS

50 cases of erythrasma were collected at random from the outpatients of Department of Dermatology, Chengalpattu govt medical college & hospital, Chengalpattu over a period of 1 year from Jan 2014 to Jan 2015 for the study.

Inclusion criteria :

1. All patients of either sex within age between 18 and 60 years
2. Patients with clinically confirmed diagnosis of erythrasma.

Exclusion criteria :

1. All patients of either sex < 18 and >60 years
2. Patients who were on treatment with systemic or topical antibiotics
3. Patients who were on treatment with topical steroids.
4. Known hypersensitivity to any of the components of the study medications
5. Severe hepatic, renal, and systemic skin diseases.
6. Pregnancy and lactation

During Study

1. If patient develops severe side effects/intolerant during the treatment
2. If patient wants alternate medicine during the study
3. If patient discontinues the treatment

With informed consent the cases were chosen for the study with the clinical diagnosis.

Subsequently careful history was elicited with particular reference to the following:

- (i) Age, Sex of patient
- (ii) Symptoms and duration of disease.
- (iii) Symptoms related to predisposing conditions.

A detailed systemic and dermatological examination were done.

Routine analysis of hemoglobin, urine, blood sugar, renal function tests, liver function tests were done in all patients.

In appropriate cases thyroid function tests and ELISA for HIV were done.

The skin lesions erythrasma were subjected to clinical examination and Wood's lamp visualization.

For Wood's lamp examination the patient was asked to come without having bath. A portable Wood's lamp was used. The patient was undressed in a dark room and the lesions were examined under Wood's lamp.

The scales from the lesion were collected by scraping. Using egg albumin the scales were fixed on to the slide. The smears were then stained by Gram method and visualised under light microscopy.

In all cases culture was done. The site of the lesion was thoroughly cleaned and scraping was done. The scales collected were inoculated using a sterile platinum loop into a medium containing Mueller - Hinton Agar enriched with blood. The inoculated plates were incubated at room temperature for 48 hours. After 48 hours the colonies which appeared were subjected to Wood's lamp examination and observed for coral red fluorescence.

After the confirmation of diagnosis, 50 patients were randomly divided into group A and group B with 25 patients in each.

Group A were treated with 2% clotrimazole cream and **Group B** with 2% fusidic acid cream for 2 weeks.

Comparison of its efficacy was based on colour intensity , demarcation and Wood's lamp reflection score.

EFFICACY PARAMETERS

Efficacy of treatment was assessed by the percentage in reduction of colour intensity, demarcation, scaling and Wood's lamp reflection score on 1st day , 7th day and 14th day with physician's global assessment score.

Grade 0 - worsened

Grade 1 – nil 0-25% reduction

Grade 2 – mild improvement -26-50% reduction

Grade 3 - moderate improvement -50-75%reduction

Grade 4 - marked improvement -76-100% reduction

The response rate { % reduction in colour intensity, scaling and demarcation } was assessed during every follow up.

Wood's lamp reflection score

Score 2- prominent red fluorescence

Score 1 – mild red fluorescence

Score 0 – no fluorescence

These score values are considered as follows complete response 0.

Partial response 0.5-1, no response 1.5 -2.

Statistical Analysis

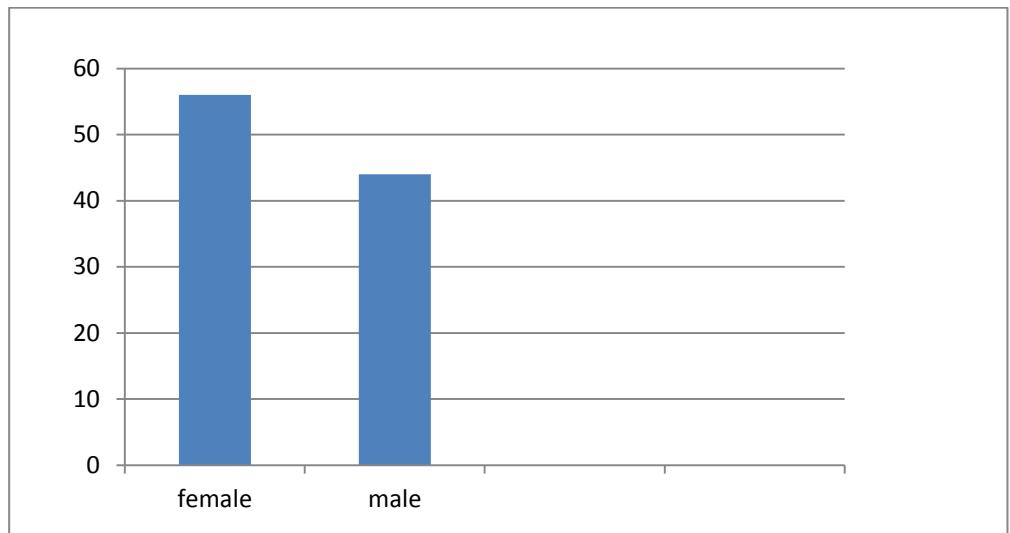
All variables were examined for outliers and non-normal distributions. The categorical variables were expressed as frequency and percentage. The quantity variables were expressed as mean and standard deviation. Descriptive statistics were used to evaluate baseline characteristics .The group comparison for the categorical variables were analyzed using chi – square test and for quantity variables were analyzed using Analysis of Variance (ANOVA) and Independent student t test (or Wilcoxon rank sum test when hypothesis of normality was rejected). p - value of less than 0.05 was considered as statistically significant. The statistical analysis was carried out using statistical software SPSS 19.0.

OBSERVATIONS & RESULTS

Sex distribution

Of the 50 cases of erythrasma studied 22 were males and 28 were females. The incidence of males was 44% and females was 56%.

Following bar diagram shows percentage of sex distribution



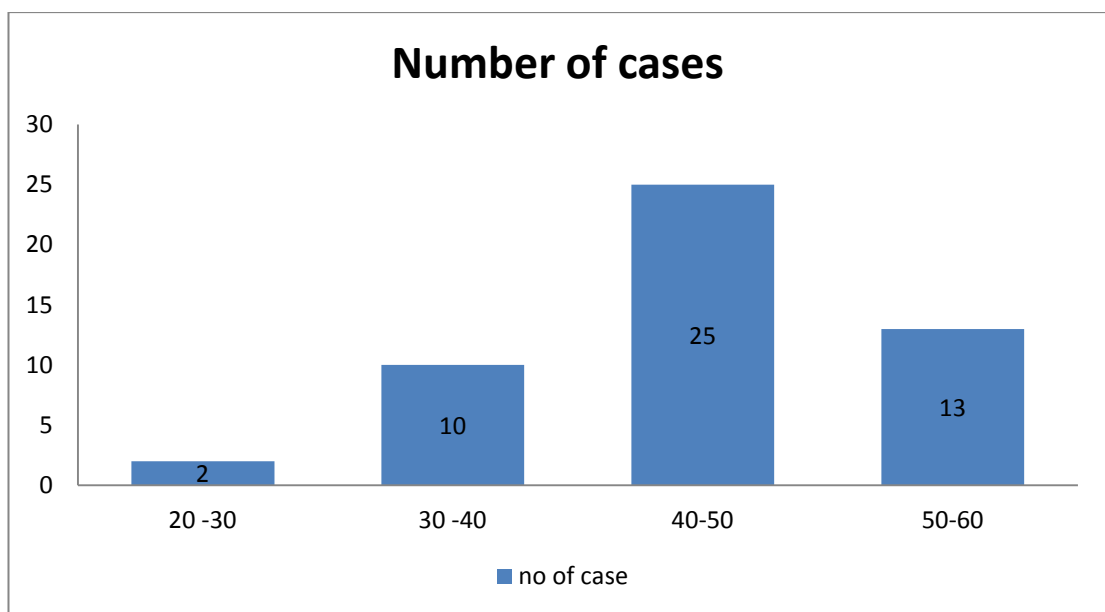
Age distribution

Age distribution in the study varied from 18 yrs to 60 yrs.

Table - I Age distribution

Age in years	No. of cases	Percentage
20 – 30	2	4
30 - 40	10	20
40 -50	25	50
50 - 60	13	26
Total	50	100

GRAPH SHOWING AGE DISTRIBUTION



50% of the cases were in the age group of 40- 50 years.

Symptoms

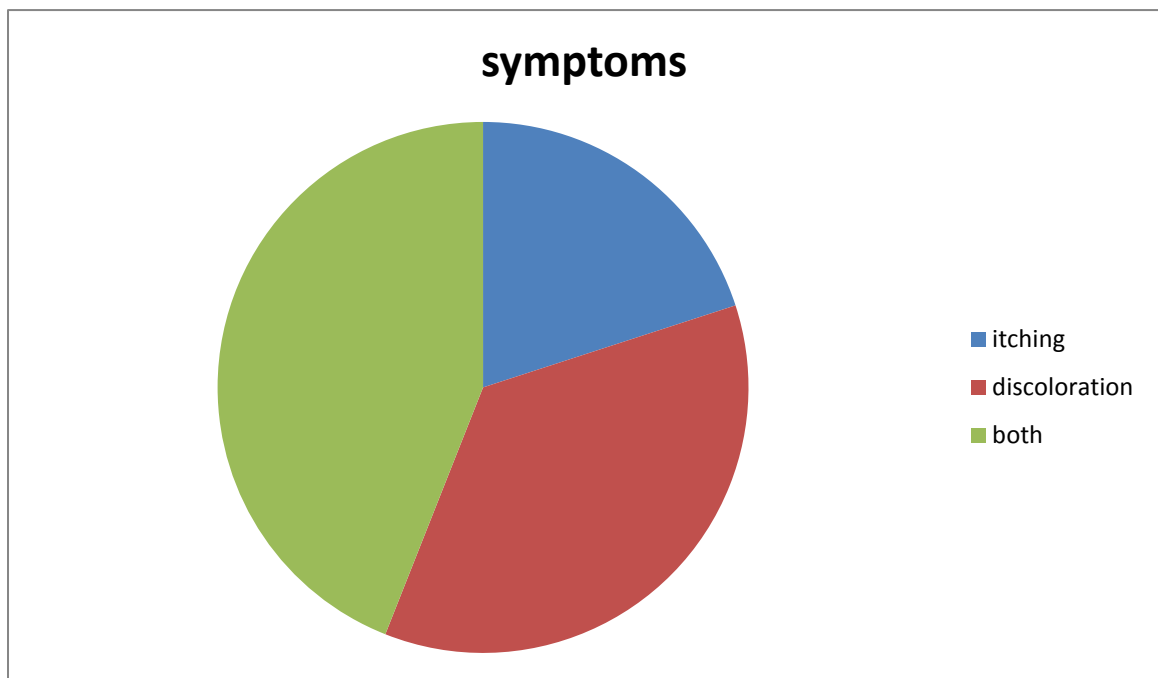
Itching and discolouration of the flexures were the predominant symptoms of erythrasma.

Table 2 - symptoms

Symptoms	No. of cases	Percentage
Itching	10	20
Discolouration	18	36
Both	22	44
Total	50	100

44% of the cases presented with both itching and discolouration.

GRAPH SHOWING SYMPTOMS



36 % of the cases presented with cosmetic problem of discolouration.

22% of the cases presented with itching alone.

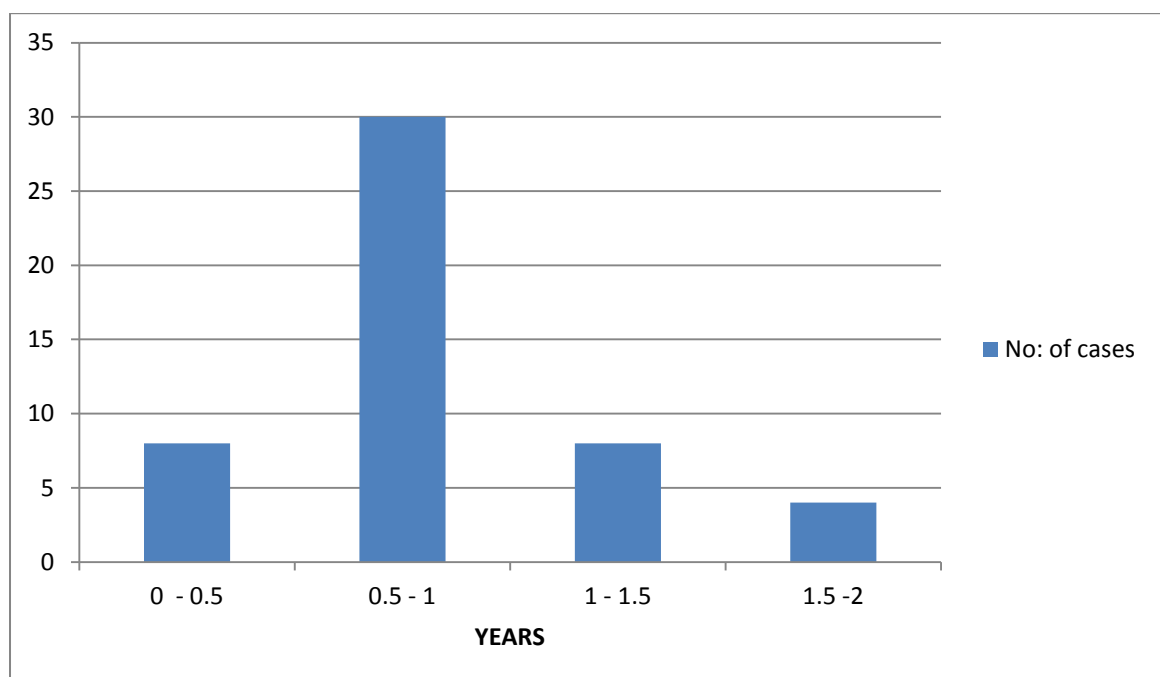
Duration of the disease

In 72% of cases the duration of disease varied between 6 months and 2 years.

Table 3- duration

Duration in years	No. of cases	Percentage
0 – 0.5	8	16
0.5 - 1	30	60
1 -1.5	8	16
1.5 - 2	4	8
Total	50	100

GRAPH SHOWING DURATION OF LESION



Maximum number of patients showing duration between 6months – 1year.

Colour of the lesion

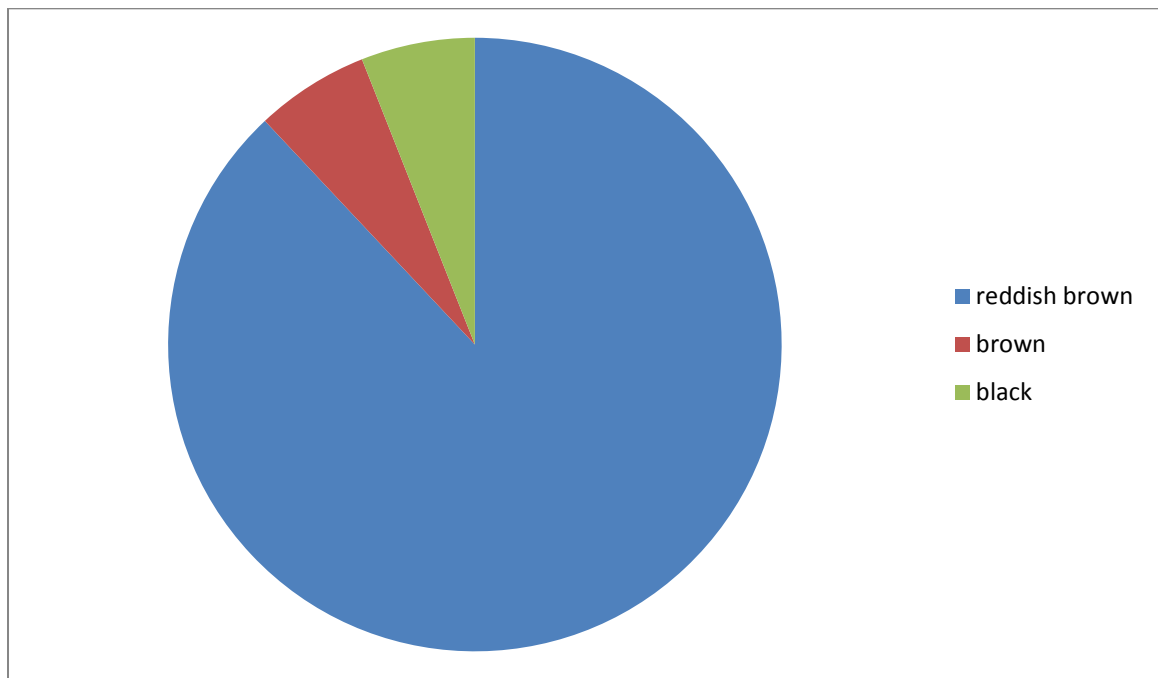
The various colours of erythrasma lesions observed

Table - 4 Various colours of the lesion observed

Morphology	No. of cases
Reddish brown	44
brown	3
black	3

Majority were of reddish brown.

GRAPH SHOWING COLOURS OF THE LESIONS



Majority of the cases observed were reddish brown (fig :1).The remaining small percentage of brown (fig :2) and black type.

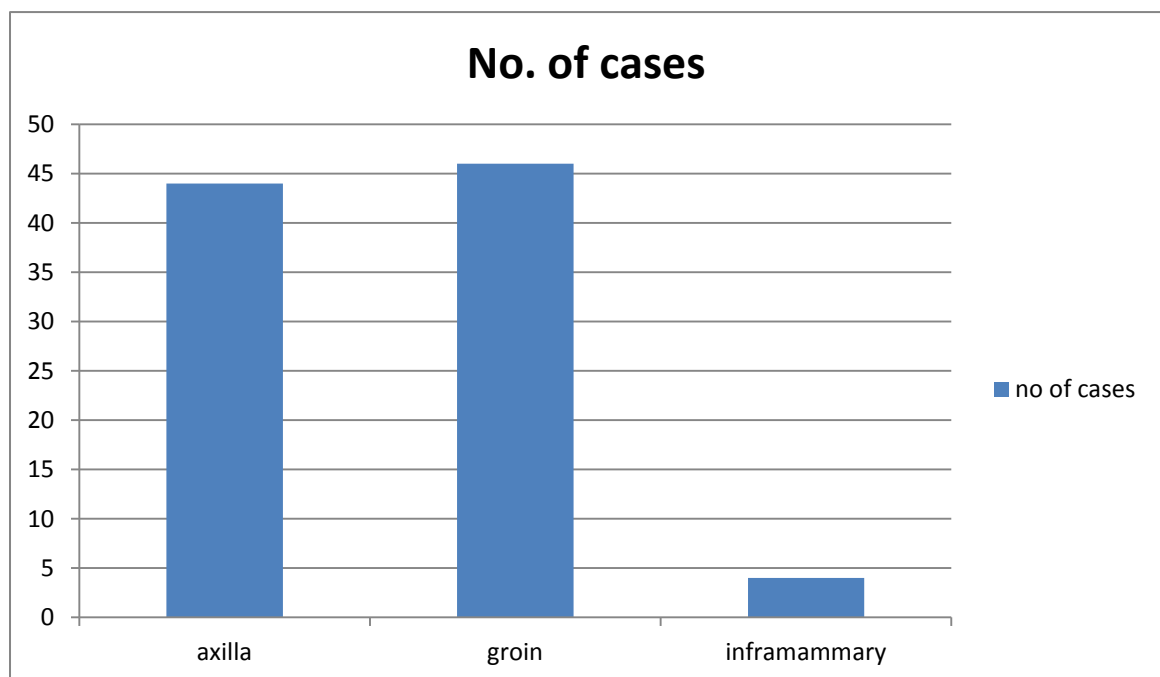
Distribution of lesions

Table 5 – Distribution of lesions

Distribution	No. of cases
Axilla	44
Groin	46
Inframammary	4

Most of the people had groin involvement [fig 2] followed by axilla [fig 3].
A few presented with inframammary area involvement [fig 4].

GRAPH SHOWING DISTRIBUTION OF LESIONS



Majority of the patients showed groin involvement.

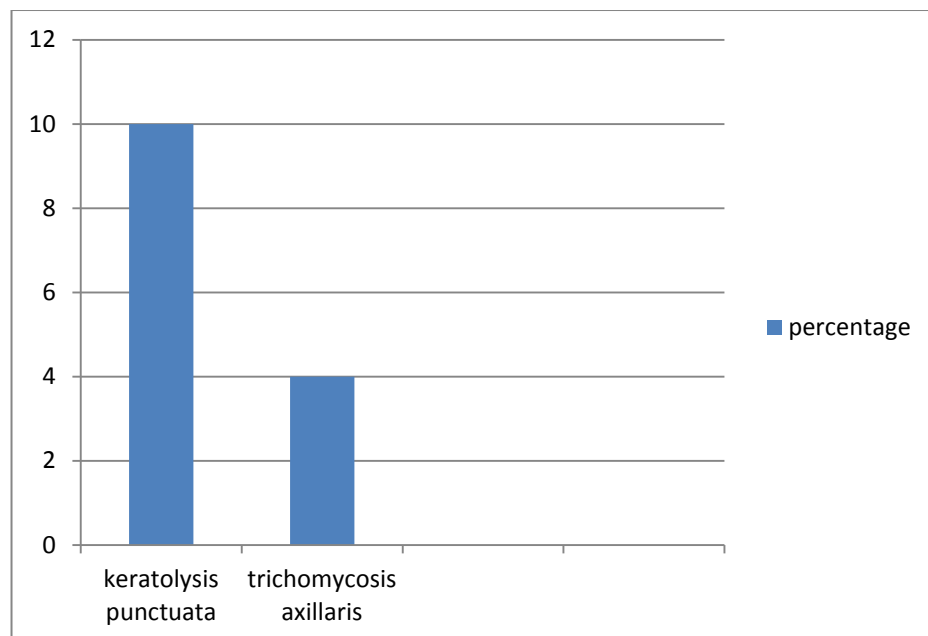
Associated corynebacterial infections.

Keratolysis punctata [fig 5] was seen in 5 of the cases and trichomycosis axillaris [fig 6] in two of the patients .

Table 6 – associated corynebacterial infections

Infections	No. of cases	percentage
Keratolysis punctata	5	10
Trichomycosis axillaris	2	4

GRAPH SHOWING NUMBER OF CASES ASSOCIATED WITH OTHER CORYNEBACTERIAL INFECTIONS



Other corynebacterial infections can be associated.

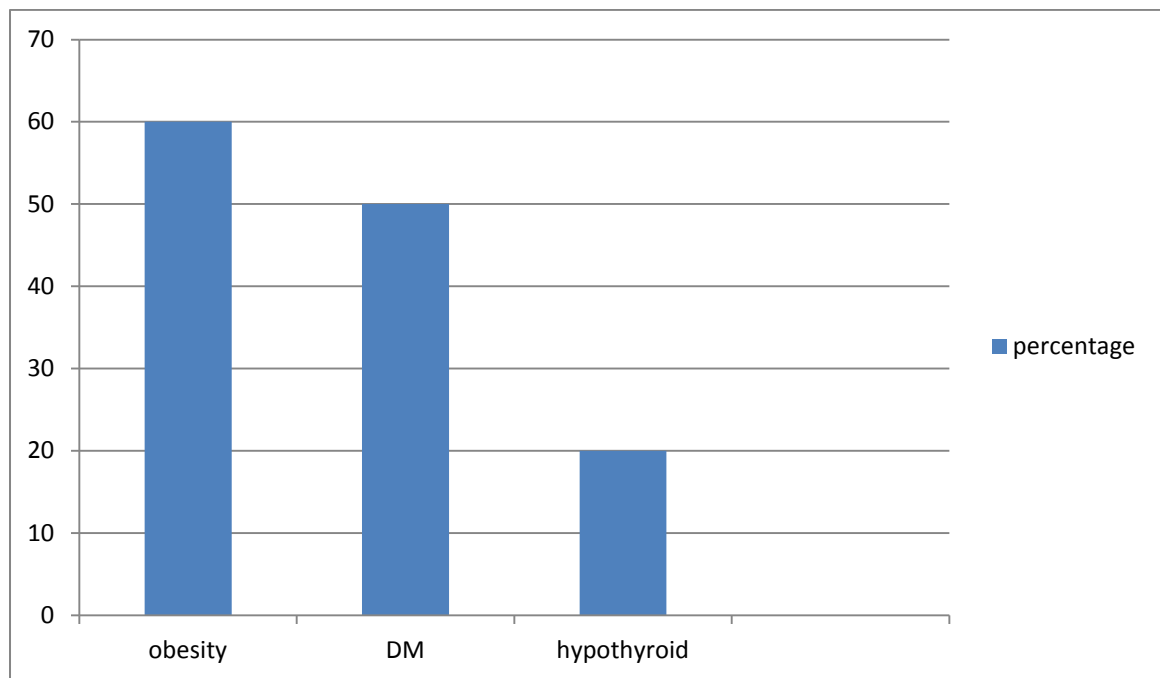
Associated systemic conditions

Among systemic conditions, obesity was associated with 60 % of cases. Diabetes mellitus was associated with 50% of cases and hypothyroidism in 20 % of cases.

Table 7—associated systemic diseases.

Systemic diseases	No. of cases	Percentage
Obesity	30	60
Diabetes mellitus	25	50
Hypothyroidism	10	20

**GRAPH SHOWING PERCENTAGE OF CASES ASSOCIATED WITH
SYSTEMIC DISEASES**



Majority are associated with obesity.

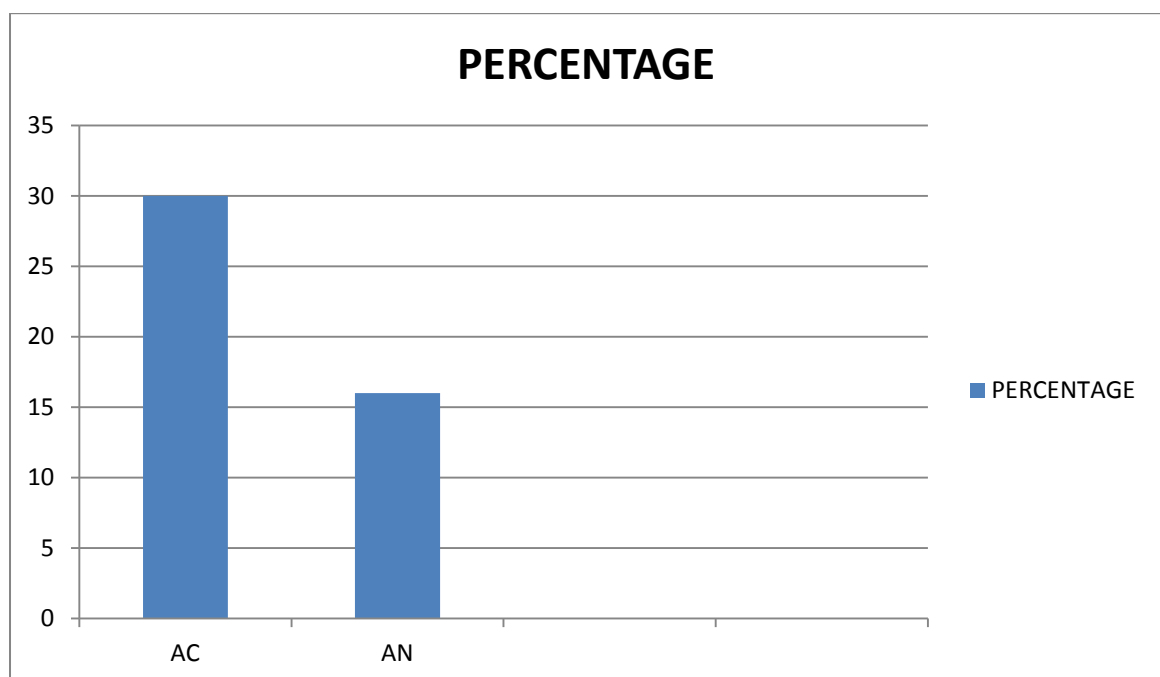
Other skin lesions associated with erythrasma

As obesity was a major factor associated, patients also presented with acrochordons [fig 7] and acanthosis nigricans. Among 50 patients, 15 patients had skin tags and 8 patients had acanthosis nigricans.

Table 8- associated skin lesions

Skin lesions	No. of cases	Percentage of cases
Acanthosis nigricans	8	16
Acrochordons	15	30

GRAPH SHOWING ASSOCIATION WITH OTHER SKIN LESIONS



30 % associated with acrochordons and 16 % associated with acanthosis nigricans.

INVESTIGATIONS

Complete Hemogram

In 50 cases recorded, anemia was seen in 5 cases leukocytosis was seen in 7 patients.

Blood Sugar : 15 cases showed hyperglycemia which were later confirmed by glucose tolerance test. 10 cases revealed diabetes mellitus.

Blood cholesterol: 5 cases were associated with hypercholesterolemia.

Thyroid Function test: Revealed hypothyroid status in 10 cases.

Elisa for HIV : positive in 3 cases.

Wood's lamp Examination : Portable Wood's lamp was used. The patient was advised to come without having bath. Coral red fluorescence (Fig 9) was observed in all.

Gram Stain: The scales were scraped and fixed on to slide using egg albumin and stained by Gram method. Gram positive coccobacilli were seen in all cases (Fig 10).

Skin biopsy

Histologically there was hyperkeratosis with basket weave stratum corneum, acanthosis and papillomatosis. There was increased pigment in the basal cell layer. Sparse inflammatory infiltrate was present in the upper dermis and around blood vessels. (fig 11)

Culture

The scales were collected and inoculated into a medium of Mueller Hinton Agar enriched with blood. Small pale grey convex colonies (Fig.12) appeared after 48 hours in only 4 cases out of 50 cases inoculated.

Treatment

Among 50 cases with erythrasma, 25 patients treated with topical 2 % clotrimazole cream and the remaining 25 patients with 2 % fusidic acid cream. In addition they were given antihistamines in case if itching is present.

These patients are compared on the basis of colour intensity, demarcation, scaling and Wood's lamp reflection scores on 1st, 7th and 14th day.

REDUCTION IN PERCENTAGE OF COLOUR INTENSITY

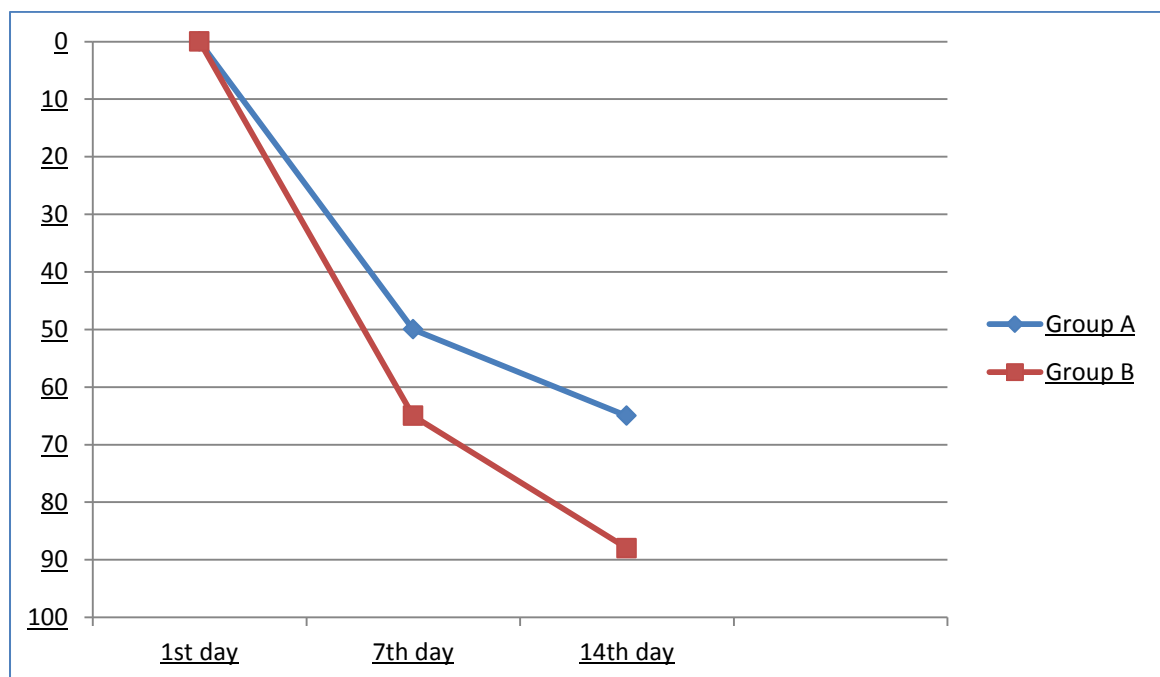
Table 9- comparing reduction in percentage of colour intensity in two groups

Day	Group A 2% clotrimazole cream	Group B 2% fusidic acid cream	p value
1	0	0	0
7	50.32±17.64	64.85 ± 18.35	0.0064
14	65.50 ±21.21	87.78±20.75	0.005

In patients in Group A, at the end of 7th day there was 50% reduction in the colour intensity. At the end of 14th day the reduction in colour intensity was 84%.

In patients in Group B , at the end of 7th day there was 65 % reduction in colour intensity. At the end of 14th day, the reduction in colour intensity was 88%.

GRAPH SHOWING REDUCTION IN PERCENTAGE OF COLOUR INTENSITY



This graph shows variation in the reduction of percentage of colour intensity in 2 groups.

REDUCTION IN PERCENTAGE OF DEMARCATION

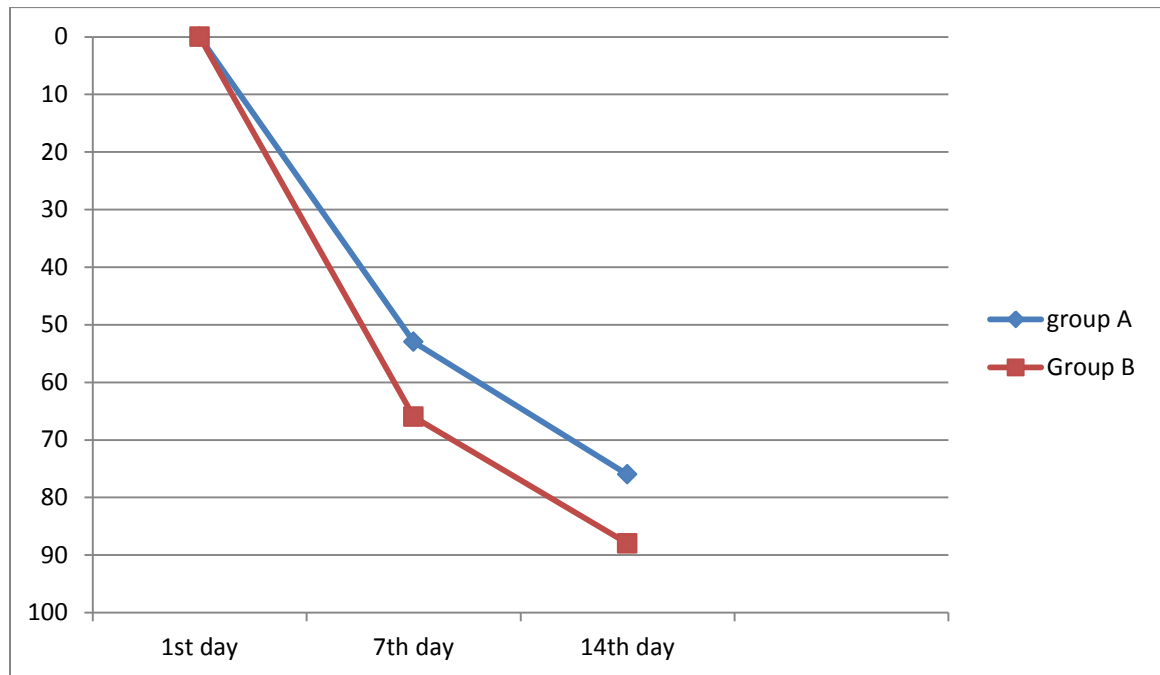
Table 10-comparing reduction in percentage of demarcation in two groups

Day	Group A 2% clotrimazole cream	Group B 2% fusidic acid cream	p value
1	0	0	0
7	53.84±17.35	66.53±22.54	0.0304
14	76.54±12.54	88.54±11.46	0.0009

At the end of 7th day ,Group A showed 53 % reduction in percentage of demarcation and at the end of 14th day they showed 76 % reduction in percentage of demarcation.

At the end of 7th day , group B showed 66 % reduction in percentage of demarcation and at the end of 14th day they showed 88% reduction in percentage of demarcation.

GRAPH SHOWING PERCENTAGE IN REDUCTION OF DEMARCATION



This graph shows variation in percentage in reduction of demarcation in the 2 groups.

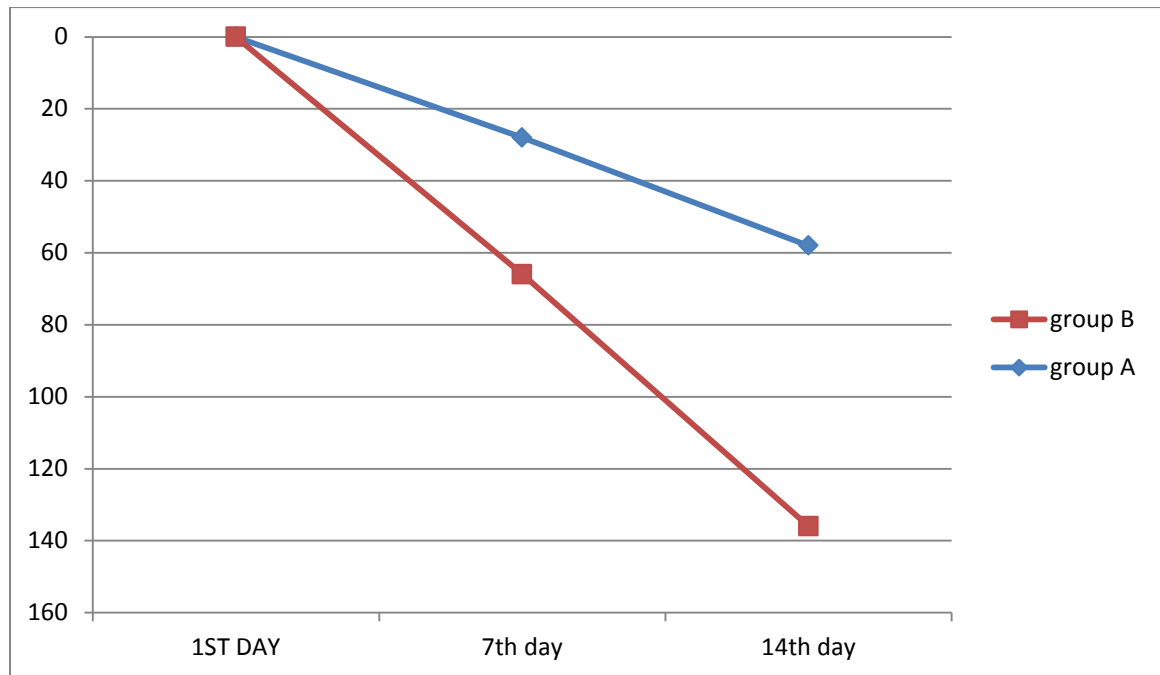
REDUCTION IN PERCENTAGE OF SCALING

Table 11-comparing reduction in percentage of scaling in two groups

Day	Group A (2% clotrimazole cream)	Group B (2% fusidic acid cream)	p value
1 st day	0	0	
7 th day	28.5± 11.32	38.5 ± 12.51	0.0046
14 th day	58.32± 19.66	78.25 ± 15.62	0.0002

Group A show 29 % reduction on 7th day and 58 % on 14th day. But **group B** showed 38% on 7th day and 58% reduction on scaling on 14th day.

GRAPH SHOWING PERCENTAGE OF REDUCTION IN SCALING



This graph shows there was significant reduction in percentage of scaling between group A and group B on 7th and 14th day of treatment.

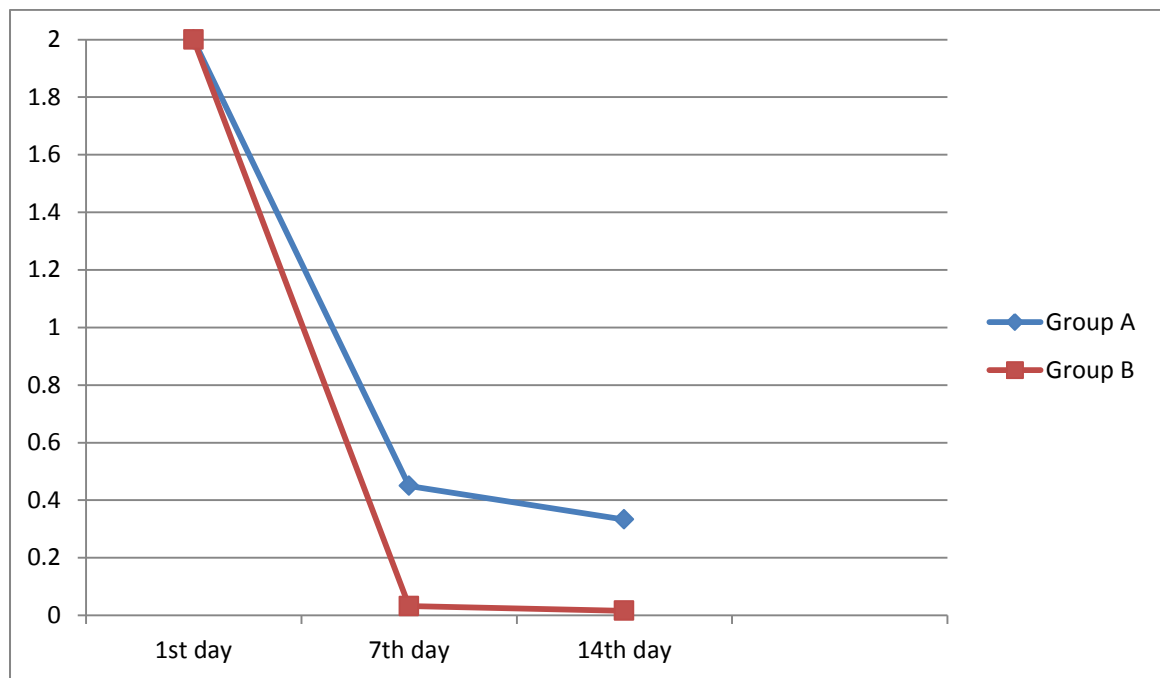
REDUCTION IN WOOD'S LAMP REFLECTION SCORE

Table 12-comparing reduction in Wood's lamp reflection score

Day	Group A [2% clotrimazole cream]	Group B [2% fusidic acid cream]	p value
1	2	2	
7	0.450±0.141	0.032±0.032	0.001
14	0.333±0.105	0.016±0.016	0.0001

Group B showed statistically significant reduction in Wood's lamp reflection score on 7th day and 14th day compared to Group A.

GRAPH SHOWING REDUCTION IN WOOD'S LAMP REFLECTION SCORE.



In this score, group B was better.

SIDE EFFECTS

Local side effects like erythema, burning sensation , hypersensitivity and allergic contact dermatitis may occur. But in the present study none of the side effects were observed.

Tolerance of patients were good in both groups.

RESPONSE TO THERAPY

Table 13 –physician’s global response

Grade	Response	2% clotrimazole cream	2% fusidic acid cream	Total
0	worsened	-	-	-
1	Nil	-	-	-
2	Mild	2	-	2
3	Moderate	8	4	12
4	Marked	15	21	36
	Total	25	25	50

According to this study, out of 25 patients in **Group A** , 2 patients showed mild response , 8 patients showed moderate response and 15 patients show marked response.

Out of 25 patients in **Group B** , 4 patients showed moderate response and 21 patients showed marked response.

DISCUSSION

Sex Distribution

In this study , there were 28 female and 22 male patients showing that the incidence of erythrasma is more in females than in males. In literature erythrasma have equal sex incidence was reported by Gary L Darmstadt et al ^[28] and it is more common in men by Peter K Lee et al ^[39]. This increased incidence may be due to the obesity commonly observed in females more than forty years.

Age Distribution

The most common age group affected were between 40 - 50 years in which half of cases occurred. 48 cases (86%) occurred in the 30 - 60 years age group. The youngest age group observed was 21 years and oldest was 60 years.

This correlates with the literature that incidence of erythrasma increase with age as reported by Gary L Darmstadt et al ^[28] and Laube S ^[6].

The prevalence of metabolic derangements like diabetes mellitus, obesity and hypothyroidism show an increase in middle age group which might be the reason for the occurrence of erythrasma in them.

Also the presence of lipid in apocrine secretion after puberty may also influence the above finding.

Symptoms

In this study 22 patients (44%) had itching and discolouration of flexures as their predominant complaint. It was asymptomatic in 18 cases (36%) who reported for the cosmetic inconvenience.

In temperate climates the erythrasma lesions were symptomless as reported by RJ Hay and BM Adrians ^[16] but in tropics, irritation of lesions occur leading to scratching.

The increased sweating and maceration in the flexures due to obesity might be the reason for itching in majority of cases.

Duration of disease

It is shown in this study that erythrasma is a chronic disease and it has remissions and relapses. These relapses were associated with the hot and humid tropical climate due to increased sweating and thereby maceration.

Presence of disease in family members

12 patients (24%) had family members who were also diagnosed as erythrasma. This indicates that the disease is not contagious but the common living conditions and similar predisposing factors in families results in the increased incidence of erythrasma among family members.

Dermatological lesions

In literature the most common type reported was the reddish brown type which was also the commonest in this study. It was seen in 44 patients (88%). 3 patients with brownish macular lesion and 3 with blackish coloured lesions.

Distribution of lesions

In this study , groins were the most common site to be affected followed by axilla bilaterally and symmetrically. In literature also ,erythrasma was described to occur most commonly in the groins by RJ Hay and BM Adrians ^[15]. All the intertriginous areas were affected.

Associated corynebacterial infections

In this study, dermatophytosis, candidiasis and pityriasis versicolour are ruled out. Only keratolysis punctata and trichomycosis axillaris were taken into account.

Shelley et al in 1982 described the coexistence of erythrasma with pitted keratolysis and trichomycosis axillaris ^[31]. Concomitant erythrasma and dermatophytosis of groin was reported by Schlappner et al in 1979 ^[10]. In 2004, Karakatsanis G was the one to describe the coexistence of pityriasis versicolour and erythrasma ^[11].

The coexistence of the above infections with erythrasma indicates that common predisposing factors of moisture and obesity are involved in these conditions.

Associated systemic disorders

The literature reports of Haroon TS ^[13] and Scheinfeld NS ^[15] showed that the increased frequency of obesity and diabetes in the patients associated with

erythrasma .This may be related to the high levels of cutaneous free glucose occurring in diabetes mellitus.

The association of hypercholesterolemia in 5 patients (10%) in the study group suggests that an increase in cutaneous lipid may possibly promote the growth of lipophilic *Corynebacterium minutissimum*.

Hypothyroidism and obesity may be the underlying cause in them which may predispose to erythrasma.

The association of thyroid disorders and diabetes suggest that a possible autoimmune mechanism may play a predisposing role to erythrasma.

Investigations

Anemia was recorded in 5 cases and leucocytosis was seen in 7 cases. There was no reactive leucocytosis as this bacteria is usually not invasive and remains mainly in stratum corneum.

The literature states that erythrasma prevalence is not increased in immunosuppressed patients ^[42]. Only 3 cases were positive for HIV by ELISA in this study.

Specific investigations

The procedures like Wood's lamp and Gram stain smear were the one to prove that etiological agent is *Corynebacterium minutissimum* by demonstrating its coproporphyrin production by coral red fluorescence and visualization of gram positive coccobacilli.

These two tests gave consistently positive results in almost all cases and the diagnosis of erythrasma was confirmed following which they were taken for therapeutic study.

Treatment

Though both topical 2% clotrimazole cream and 2% fusidic acid cream showed greater reduction in colour, intensity and Wood's lamp reflection score in erythrasma. At the end of 2nd week, 2% fusidic acid cream showed significant reduction in intensity, demarcation and Wood's lamp reflection score.

In a double-blind, placebo-controlled study in which oral erythromycin and topical 2% fusidic acid cream were used in 86 cases of erythrasma, it was found that the rate of complete response was 77% in the erythromycin group, 87% in the fusidic acid 2% cream group and 42% in the placebo group, and no statistically significant difference was found between these treatment modalities ^[57]. In another study, a twice-daily 14-day application of 2% fusidic acid cream had the success rate of up to 89%, and no recurrence was seen in the 40th post-treatment week ^[58].

In the present study, the reduction in colour intensity from baseline to 2 weeks was significantly greater in 2% fusidic acid than 2% clotrimazole cream {89% vs 76%}. Though both the groups showed reduction in colour intensity, rapid onset of reduction within first week was shown by 2% fusidic acid cream.

The reduction in demarcation from baseline to 2 weeks was significantly greater in 2% fusidic acid cream than 2% clotrimazole cream {86% vs 66%}. Reduction in demarcation was rapid in the group of 2% fusidic acid cream.

The reduction in percentage of scaling from baseline to 2 weeks was significantly greater in 2% fusidic acid cream than 2% clotrimazole cream { 78% vs 58% }. Reduction was greater with 2% fusidic acid cream. But compared to other parameters ,the reduction in percentage of scaling was much lesser.

The reduction in Wood's lamp reflection score was significantly greater in 2% fusidic acid cream than 2% clotrimazole cream .Wood's lamp reflection score was almost zero in 1st week itself or 2% fusidic acid cream. In Oktay vaci et al study , 2% fusidic acid cream showed almost complete reduction in Wood's lamp reflection score ^[61].

Response of treatment to 2 % fusidic acid cream and 2% clotrimazole cream was moderate to marked . But marked response was seen in increased number in group of 2 % fusidic acid cream compared to 2% clotrimazole cream. Few patients in 2% clotrimazole cream show mild improvement.

Side effects like burning sensation, irritation or allergy contact dermatitis was not observed in any of the study groups. Compliance and tolerance were good in both groups.

In general , topical 2% fusidic acid cream was found to be more effective than 2% clotrimazole cream in patients with erythrasma. It shows that antibacterial activity is more with 2% fusidic acid cream compared to 2% clotrimazole cream. Topical 2% clotrimazole cream is effective when there is associated fungal infection. Patients were taken for study after ruling out fungal infections and hence the decreased efficacy of 2% clotrimazole cream.

CONCLUSION

The following conclusions were drawn through the study regarding erythrasma

1. More common in females.
2. More common in the age group 40 -50 years.
3. Duration of lesions vary from 6 months to 2years.
4. Discolouration and itching were the predominant symptoms.
5. Morphologically reddish brown macular lesions are common.
6. Groin is the most common site of involvement.
7. Other corynebacterial infections like keratolysis punctata and trichomycosis axillaris could be associated.
8. Systemic disorders like obesity .diabetes mellitus and hypothyroidism could be associated.
9. Gram stain and Wood's lamp examination were more useful aids in diagnosis.
10. 2 % fusidic acid cream was effective than 2% clotrimazole cream in its treatment.
11. Tolerance and compliance were good in both 2% fusidic acid cream and 2% clotrimazole cream.
12. Efficacy was seen rapidly with 2% fusidic acid cream.
13. Antibacterial activity towards corynebacterium minutissimum was more with fusidic acid than clotrimazole.

FIGURE - 1



FIGURE - 2



FIGURE - 3

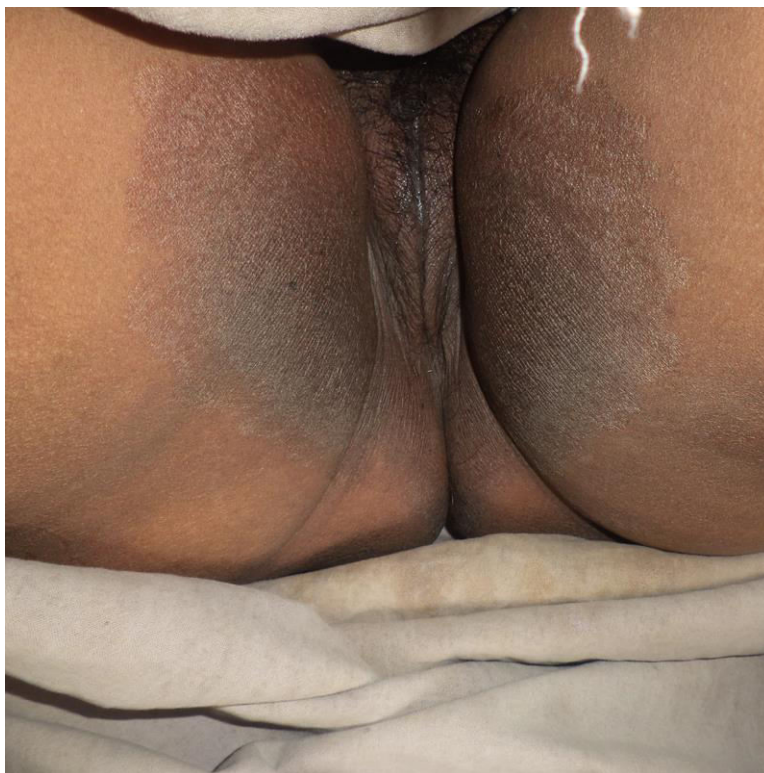


FIGURE - 4



FIGURE - 5



FIGURE - 6



FIGURE - 7



FIGURE - 8



FIGURE - 9

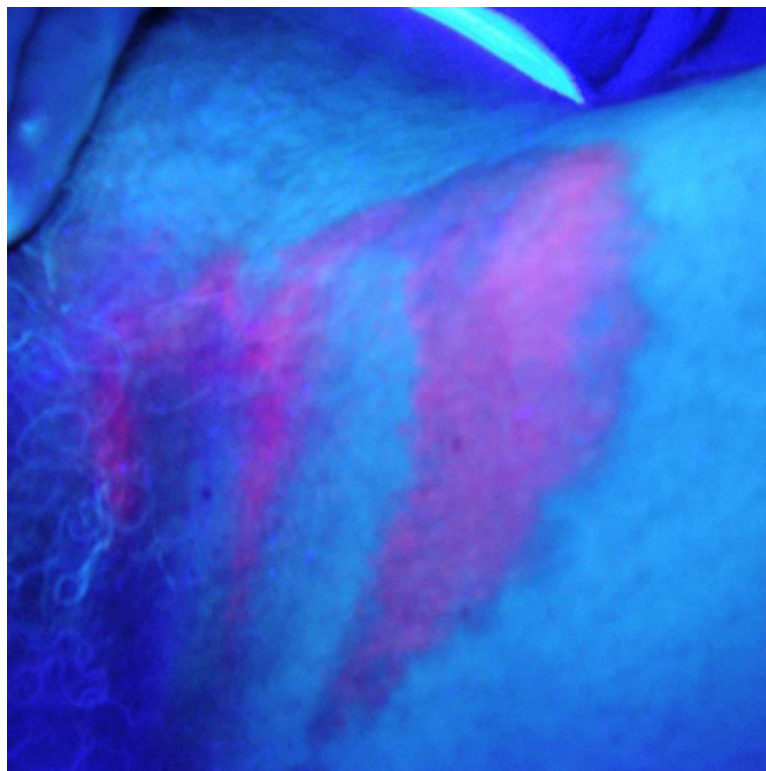


FIGURE - 10



FIGURE - 11

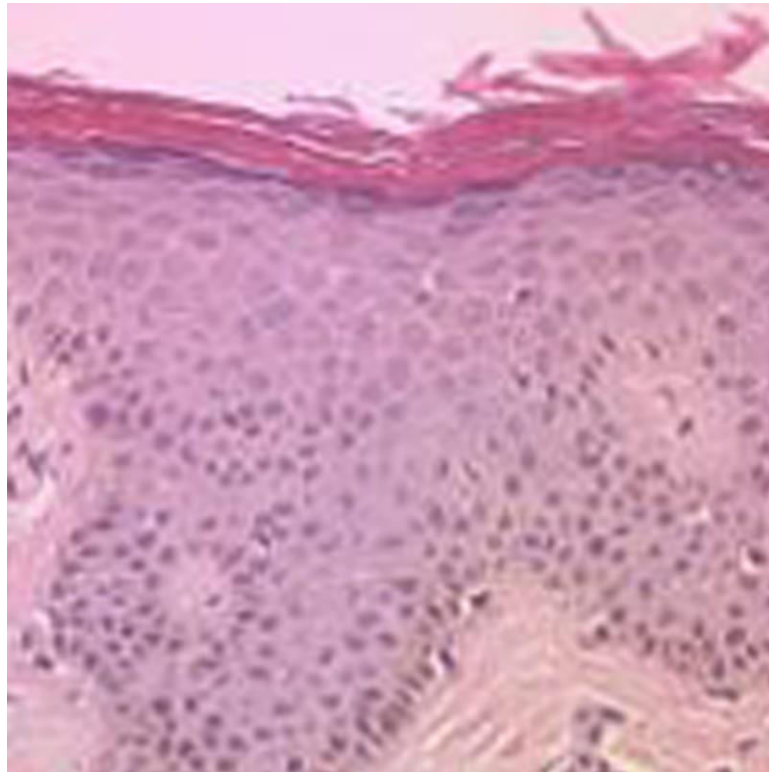


FIGURE - 12



FIGURE - 13



FIGURE - 14



FIGURE - 15



FIGURE - 16

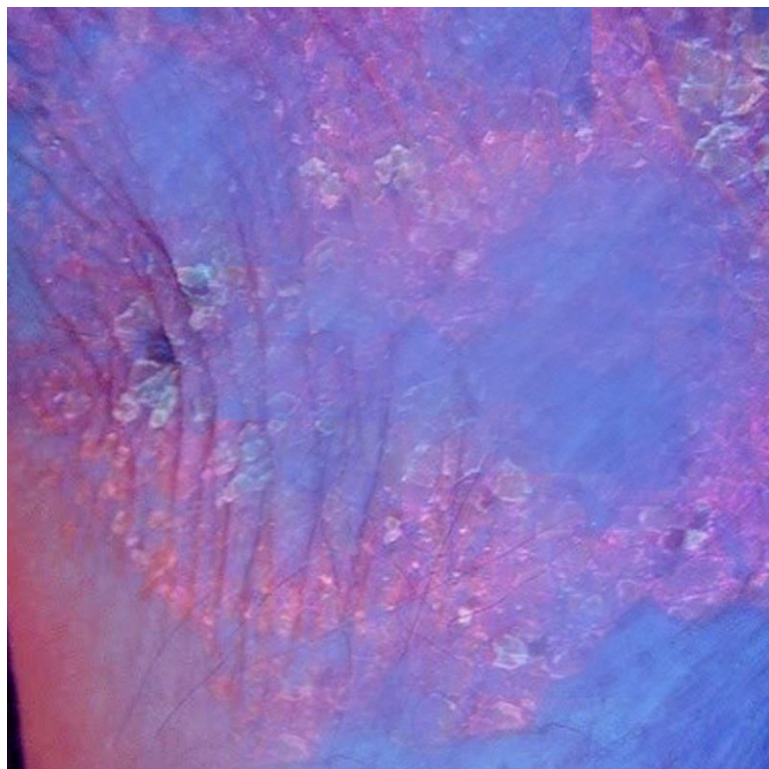


FIGURE - 17



FIGURE - 18



FIGURE - 19

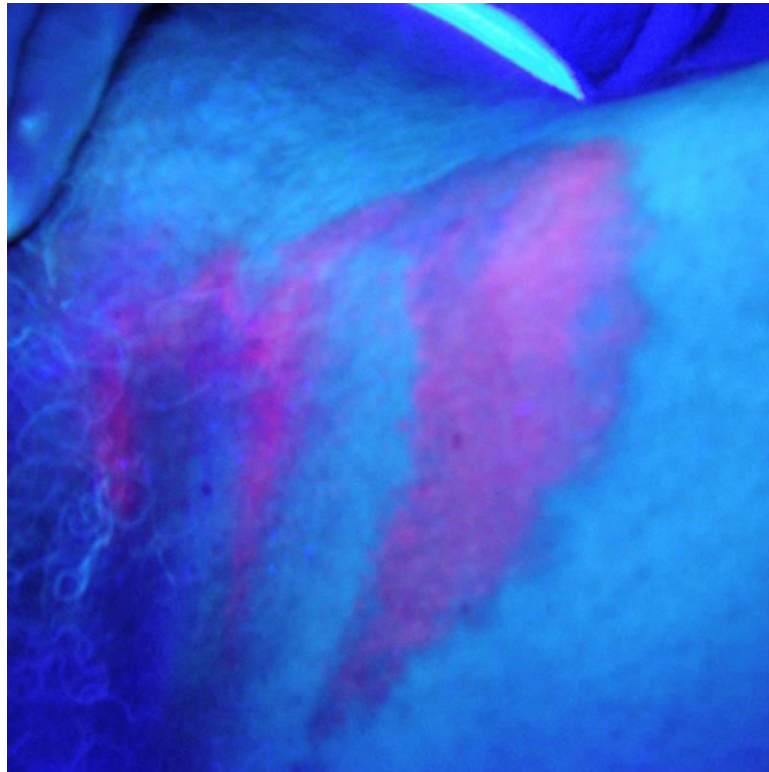
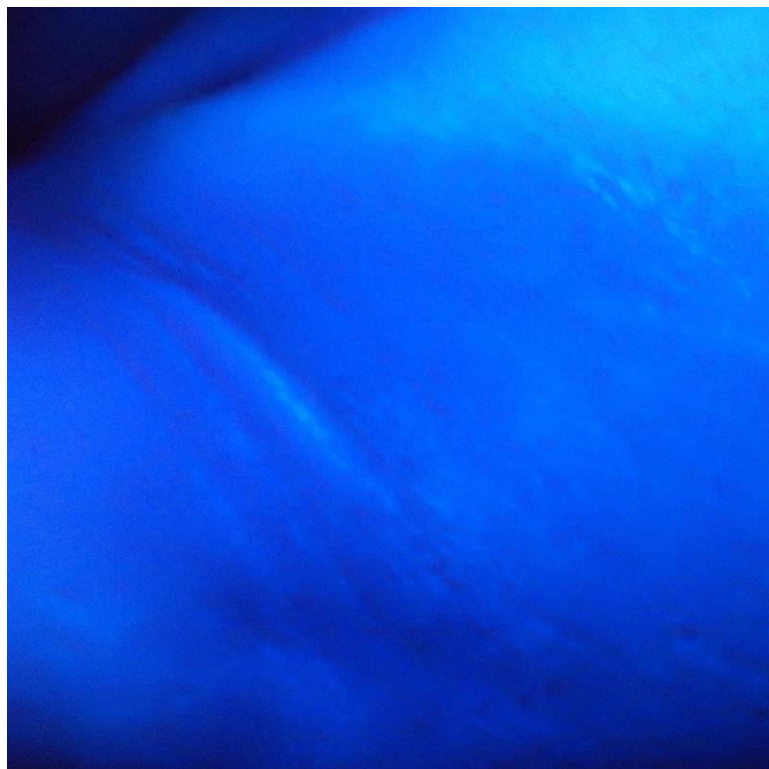


FIGURE - 20



REFERENCES

1. Maibach HI, Raza A : Bacterial infections of skin in Moschella SL, Hurley JH (eds): Dermatology, Ed 3. Philadelphia, WB Saunders Co, 1992, pp 731 - 732.
2. Kamalam. A, Thambiah. A.S., Bagavan das. M. and Govindaraju. S Mycoses in India-Study in Madras. Transactions of the Royal Society of Tropical Medicine and Hygeine 1981, Vol.75, 92-100.
3. Marks. R, N.D. Ramnarain, B.Bhogal and N.T.Moore. The erythrasma micro organism insitu-studies using the skin surface biopsy technique. J. Clin. Pathol. 1972 September, 25(9): 799-803.
4. Sarkany I, Taplin D, Blank H. The etiology and treatment of erythrasma. .Invest Dermatol. 1961; Vol.37, pp.283-290.
5. Sarkany I, Taplin D, Blank H. Incidence and Bacteriology of erythrasma. Arch Dermatol 1962 May; 85: 578-82.
6. Laube S. Skin Infections and ageing. Ageing Res Rev 2004 Jan; 3(1): 69-89.
7. Morales-Trujillo ML, Arenas R, Arroyo S. [Interdigital erythrasma: clinical, epidemiological and microbiologic findings]. *Actas Dermosifiliogr.* Jul-Aug 2008;99(6):469-73.
8. Holdiness MR. Erythrasma and common bacterial skin infections. Am Fam Physicians 2003 Jan 15; 67(2): 254.
9. Bowyer A, Mc Coll I. Erythrasma and pruritusani. Acta Derm Venereol 1971; 51(6) 444-7.

10. Schlappner OL, Rosenblum GA, Rowden G, Phillips TM. Concomitant Erythrasma and dermatophytosis of groin. *Br.J. Dermatol* 1979 Feb; 100(2):147-51
11. Karakatsanis G, Vakirlis E, Kastoridou C, Devliotou-Pangiotidou D coexistence of pityriasis versicolour and Erythrasma. *Mycoses* 2004 Aug; 47(7):343-5.
12. Somerville DA, Lancaster-Smith M. The anerobic cutaneous microflora of diabetic subjects. *Br. J. Dermatol* 1973, Vol.89; 395-400.
13. Haroon TS , Diabetes and Skin-a review. *Scott Med J.* 1974 Nov. 19; 257-67.
14. Montes LF, Dobson H, Dodge BG, Knowles WR. Erythrasma .
15. Scheinfeld NS. Obesity and dermatology. *Clin Dermatol* 2004 Jul-Aug; 22(4):303-9.
16. Author RJ Hay and BM Adrians. Textbook of Dermatology Rook edited by Tony Burns, Stephen Breathnach, Neil Cox, Christopher Griffiths. 7th edition, Vol.2 Bacterial infections.
17. Sarkany I, Taplin¹⁶. Sarkany I, Taplin D, Blank H. Erythrasma-Common bacterial infection of skin *JAMA* 1961 Jul 15; 177; 130-2.
18. Montes LF, McBride ME, Johnson WP, Owens DN, Knox JM. Ultrastructural study of host bacterium relationship in erythrasma. *J. Bacteriol* 1965 Nov; 90(5):1489-91.
19. Marks R. Keio. Seeing through the stratum corneum. *J. Med.* 2000 Jun. 49:80-3.
20. Montes LF, Black SH, McBride ME. Bacterial invasion of stratum corneum in erythrasma, ultrastructural evidence of keratolytic action exerted by corynebacterium minutissimum. *J. Invest Dermatol.* 1967, Nov; 49; 474-85.
21. Hartmann AA. The influence of various factors on the human resident skin flora. *Sem in Dermatol* 1990 Dec. 9 : 305 - 8.

22. Noble W-C and Somerville D.A., Physical features p3-23; *Corynebacteria as Pathogens*; p-100-120, In: *Microbiology of Human skin*-London, Philadelphia, Toronto, Saunders, 1974.
23. Golledge CL, Phillips G. *Corynebacterium minutissimum* infection. *J. Infect* 1991, Jul 23: 73-6.
24. Stephen A Berger, Alfred Gorea, Jona Stadler, Michael Dan. Recurrent breast abscesses caused by *C.minutissimum*. *Journal of clinical. Microbiology*, Dec 1984, P.1219 - 1220.
25. *Andrews' diseases of skin-clinical dermatology*; 9th edition Edited by Richard B.Odom, William. D.James, Timothy G.Berger. *Bacterial infections* Page 326.
26. Cabo H, Franco de Montes de Oca N, Tzovanis Mc, Gallardo H. Generalised erythrasma. *Med Cutan Ibero Lat Am* 1983; 11(2): 129-32.
27. Tschen JA, Ramsdell WM. Disciform erythrasma. *Cutis* 1983 May; 31(5): 541-2,547.
28. *Pediatric Dermatology* 3rd edition: Edited by Lawrence A.Schachner and Ronald C Hansen. *Bacterial infections* by Gary L. Darmstadt, Wesley king Galen and Gayle Fischer. Page 1036.
29. Grigoriu D, Delacretaz J. Vesiculobullous erythrasma of feet. *Dermatologica* 1976; 152(1): 1-7.
30. Negroni P. Erythrasma of the nails. *Med Cutan Ibero Lat Am* 1976, 4(5):349-57.
31. Shelley WB, Shelley ED. Coexistent erythrasma, trichomycosis axillaris and pitted keratolysis-an overlooked corynebacterial triad? *J Am Acad Dermatol* 1982. Dec; 7(6): 752-7.

32. Guarderas J; A.Karnad, S.Alvarez, S.L.Berk. *Corynebacterium minutissimum* bacteremia in a patient with CML in blast crisis. *Diag. Microbiol. Infect. Dis.* 1986, Vol.5, pp.327-330.
33. Brian H.J; A.J.Brucker; 1985. Embolic retinopathy due to *corynebacterium minutissimum* endocarditis. *Br. J. Ophthalmol*, Vol.69, pp.29-31.
34. Wigger Alberti W, Elsnor P. Fluorescence with Wood's light. Current applications in dermatologic diagnosis, therapy, follow-up and prevention. *Hautarzt* 1997, Aug 48: 523-7.
35. Mattox TF, Rutgers J, Yoshimori RN, Bhatia NN. Nonfluorescent erythrasma of vulva. *Obstet Gynecol* 1993 May; 81(5): 862-4.
36. Padilha - Goncalves A. A single method to stain *Malassezia furfur* and *corynebacterium minutissimum* in Scales. *Rev Inst Med. Trop. Sao Paulo* 1996 Jul-Aug 38 : 299 - 302.
37. Stephen N Cohen, Dorothy Nickolai. Simple medium for pigment production by the erythrasma diphtheroid. *Appl. Microbiol* 1969 March; 17(3): 479-480.
38. Skin pathology David Weedon 2nd edition. Bacterial and rickettsial infection. Page 622.
39. Fitz patricks Dermatology in General Medicine-6th Edition: Edited by Irwin M Freedberg (et al) Vol.2, Chap. 194, Pyodermas. Author Peter KLee, Mathew T. Zipolli, Arnold N Weinberg, Morton Swartz and Richard A.Johnson Pg. 1876.
40. Aste N, Pau M. Pityriasis versicolour on groin mimicking erythrasma. *Mycoses* 2004; June; 47(5-6): 249-51.
41. Gupta S. Pityriasis rotunda mimicking tinea cruris/corporis and erythrasma in an Indian patient. *J. Dermatol* 2001 Jan; 28(1): 50-3.

42. Treatment of skin disease. 1st edition. Edited by Mark Lebwohl, Warren R Heymann, John Berth Jones, Ian Loulson. Erythrasma by Andrew G. Smith page 203.
43. Holdiness MR. Management of cutaneous erythrasma. *Drugs* 2002; 62(8): 1131-41.
44. Wharton JR, Wilson PL, Kincannon JM, Erythrasma treated with single dose clarithromycin. *Arch Dermatol* 1998 Jun; 134(6): 671-2.
45. Goodman and Gilman's The pharmacological basis of therapeutics 11th edition: edited by Laurence.L.Brunton, John.S.Lazo, Keith.L.Parker. Antifungal agents by John.E.Bennet 1230-1238
46. Drugbank. www.drugbank.ca/drugs/DB0025007.
47. Generic drugs. <http://www.ndrugs.com/?s=clotrimazole#ixzz3XZJHGUrl>
48. Kucers A.. Fusidate sodium. *In*: Kucers A, Crowe SM, Grayson ML, Hoy JF, editors. The use of antibiotics. 5th ed. Oxford: Butterworth-Heinemann; 1997. p. 580-6.
49. Hansson S, Singh R, Gudkov AT, Liljas A, Logan DT. Structural insights into fusidic acid resistance and sensitivity in EF-G. *J Mol Biol* 2005;348:939-49.
50. Tanaka N, Kinoshita T, Masukawa H. Mechanism of protein synthesis inhibition by fusidic acid and related antibiotics. *Biochem Biophys Res Commun* 1968; 30:278-83.
51. Bodley JW, Zieve FJ, Lin L, Zieve S. Formation of the ribosome-G factor-GDP complex in the presence of fusidic acid. *Biochem Biophys Res Commun* 1969; 37:437-43.
52. Collignon P, Turnidge J. Fusidic acid *in vitro* activity. *Int J Antimicrob Agents*. 1999;12 Suppl 2:S45-58

53. Vickers CF. Percutaneous absorption of sodium fusidate and fusidic acid. *Br J Dermatol.* 1969; 81:902-908
54. Turnidge J. Fusidic acid pharmacology, pharmacokinetics and pharmacodynamics. *Int J Antimicrob Agents.* 1999;12 Suppl 2:S23-34.
55. Christiansen K. Fusidic acid adverse drug reactions. *Int J Antimicrob Agents.*
56. Reimann G, Barthel B, Rockstroh JK, Spatz D, Brockmeyer NH. Effect of fusidic acid on the hepatic cytochrome P450 enzyme system. *Int J Clin Pharmacol Ther.* 1999;37:562-566.
57. Haman K, Thorn P. Systemic or local treatment of erythrasma? A comparison between erythromycin tablets and fucidin cream in general practice. *Scand J Prim Health Care.* 1991;9:35–39.
58. MacMillan AL, Sarkany I. Specific topical therapy for erythrasma. *Br J Dermatol.* 1970;82:507–509.
59. Darras-Vercambre S, Carpentier O, Vincent P, Bonneville A, Thomas P. Photodynamic action of red light for treatment of erythrasma: preliminary results. *Photodermatol Photoimmunol Photomed.* 2006 Jun. 22(3):153-6
60. Turk BG, Turkmen M, Aytimur D. Antibiotic susceptibility of *Corynebacterium minutissimum* isolated from lesions of Turkish patients with erythrasma. *J Am Acad Dermatol.* 2011 Dec. 65(6):1230-1..
61. Avci O, Tanyildizi T, Kuskü E. A comparison between the effectiveness of erythromycin, single-dose clarithromycin and topical fusidic acid in the treatment of erythrasma. *J Dermatolog Treat.* 2011 Sep 18.
62. Seville RH, Somerville A. Treatment of erythrasma in a hospital for mentally subnormal. *Br J Dermatol* 1970;82:502-6.

63. K Hamann, P Thorn .Systemic or Local Treatment of Erythrasma? A comparison between Erythromycin Tablets and Fucidin R Cream in General Practice. - Scandinavian journal of primary health care, 1991 - Taylor & Francis
64. Clayton YM, Knight AG. A clinical double-blind trial of topical miconazole and clotrimazole against superficial fungal infections and erythrasma.. Clin Exp Dermatol. 1976 Sep;1(3):225-32.
65. Yvonne m. Clayton and Bruce Connor. Comparison of clotrimazole cream, Whitfield's's ointment and Nystatin ointment for the topical treatment of ringworm infections, pityriasis versicolour, erythrasma and candidiasis. British Journal of Dermatology Volume 89, Issue 3, pages 297–303, September 1973.

**ERYTHRASMA - A CLINICAL STUDY AND A COMPARTIVE
STUDY OF TOPICAL 2% FUSIDIC ACID CREAM VS 2%
CLOTRIMAZOLE CREAM IN THE TREATMENT OF
ERYTHRASMA.**

Name:

Address:

Age:

Marital Status:

Sex :

Occupation :

Case No:

Hospital No:

HISTORY

Dark discolouration of flexures: Yes No

Duration : Yes No

Itching: Yes No

Past History

Similar illness: Yes No

DM HT TB RA Others

Family History

Similar illness Partner Parents Children Others

Drug History

Steroids: Yes No

Menstrual History

Menarche:

Periods:

Menopause:

EXAMINATION

General Examination

Built: Well Moderate Poor

Height: (m)

Weight: (kg)

BMI:

Anaemia: Yes No

Lymphadenopathy: Yes No

Systemic Examination

CVS RS ABDOMEN

CNS

Dermatological Examination

Distribution of lesion: Genitocrural Axilla Inframammary

Others:

Colour of lesion: Reddish brown Brown Black

Extent of lesion:

Nail : Normal Subungual hyperkeratosis Onycholysis

Mucosa: Normal

Associated Skin Disorders

Other Corynebacterium causing disorders: Trichomycosis axillaries
pitted keratolysis

Others

INVESTIGATIONS

Blood: Hb Urine: Albumin Sugar Deposits

Blood sugar: GTT

Serum cholesterol:

Optional

Thyroid function tests:

ELISA:

Specific

Wood's lamp Examination:

Gram's stain smear:

Culture:

Biopsy:

TREATMENT

2% clotrimazole cream / 2% fusidic acid cream

FOLLOW UP

Day	Colour intensity	Demarcation	Wood's light reflection score	Scaling
1				
7				
14				

PHYSICIAN'S GLOBAL ASSESSMENT RESPONSE

Worsened	nil	mild	moderate	marked

KEY TO MASTER CHART

Symptoms

D - Discolouration

I – Itching

B -both

Sites

G - Groin

A - Axilla

I - Inframammary

Lesion

RB- reddish brown

BR - brown

BL -black

Skin Infections

K - Pitted keratolysis

T - Trichomycosis

Associated Systemic Disorders

O - Obesity

DM - Diabetes mellitus

H – Hypothyroidism

Other skin lesions

AN – acanthosis nigricans

AC - achrochordon

Treatment

C –colour intensity

D -demarcation

W –wood's light reflection score

Assessment

R- Physician's global assessment response

MASTER CHART – GROUP A -2 % CLOTRIMAZOLE CREAM

Sl no	age	sex	dur	symptoms			morphology			site			otherinfcs		Other skin diseases		systemic			C Red% day		I Red% day		DC Red% day		S Red% day		W Red% day		R
			mon	I	D	B	BR	RB	BL	G	A	IM	T	K	AN	AC	DM	H	O	7	14	7	14	7	14	7	14	7	14	
1	28	m	3	+	-	-	-	+	-	+	-	-	-	-	-	-	+	+	+	44	86	42	83	54	88	42	82	64	100	4
2	32	f	4	-	-	+	-	+	-	+	+	+	-	-	-	-	+	+	-	45	84	43	84	48	84	40	81	68	100	4
3	35	f	7	-	+	-	-	-	+	+	-	-	-	-	-	+	+	-	+	32	66	33	71	35	74	33	72	45	84	2
4	35	f	6	-	-	+	-	+	-	+	+	-	-	-	-	-	+	-	-	38	73	37	76	40	79	37	77	57	92	3
5	36	f	9	-	+	-	-	+	-	+	+	-	-	+	-	+	+	-	+	45	83	46	88	50	84	43	84	65	99	4
6	34	m	8	-	-	+	-	+	-	-	+	+	-	-	-	-	+	-	+	37	73	36	75	38	78	36	74	56	93	3
7	31	m	5	-	-	+	-	+	-	+	+	-	-	-	-	-	-	-	-	38	74	39	78	43	84	37	77	54	94	3
8	35	m	7	+	-	-	-	+	-	+	+	-	-	-	+	+	-	-	-	36	72	36	79	40	80	35	76	55	92	3
9	39	m	10	-	-	+	-	+	-	+	+	-	-	-	+	+	+	-	+	45	88	46	89	52	87	44	84	64	100	4
10	42	f	9	-	-	+	-	+	-	+	+	-	-	-	+	+	+	-	-	44	86	43	87	46	85	43	85	63	100	4
11	41	f	7	-	+	-	-	-	+	+	+	-	-	-	-	-	+	-	-	46	89	47	90	44	87	45	86	64	100	4
12	42	f	7	-	+	-	-	+	-	+	-	-	-	-	+	-	-	-	+	35	74	32	75	36	74	34	73	63	99	3
13	45	f	9	-	+	-	-	+	-	+	+	-	-	-	+	+	+	-	+	45	86	46	92	47	89	46	84	67	100	4
14	44	f	10	-	+	-	--	+	-	+	+	-	-	+	-	-	-	-	+	31	72	28	70	32	74	32	72	44	80	2
15	41	m	11	-	-	+	-	+	-	+	+	-	-	-	-	+	+	-	-	47	89	48	83	47	87	45	86	64	99	4
16	46	m	14	-	+	-	-	+	-	+	+	-	+	-	-	-	+	+	+	46	86	46	89	45	86	44	87	63	100	4
17	47	m	15	-	-	+	-	+	-	+	+	-	-	-	-	+	-	-	+	35	77	34	75	36	75	34	74	54	86	3
18	48	f	10	-	+	-	-	+	-	+	+	-	-	-	-	-	-	-	-	44	85	46	84	45	90	43	86	62	100	4
19	49	f	16	+	-	-	-	+	-	+	+	-	-	-	-	+	-	-	+	46	88	43	85	44	86	45	83	65	98	4
20	42	f	17	-	-	+	-	+	-	+	-	+	-	-	-	-	-	-	-	36	74	37	73	37	76	35	85	53	86	3
21	52	m	19	+	-	-	-	+	-	+	+	-	-	+	-	-	+	+	+	46	86	45	92	45	86	45	84	67	99	4
22	50	m	18	-	+	-	-	+	-	+	+	-	-	-	-	-	+	+	+	36	74	34	75	35	75	35	73	53	89	3
23	51	f	10	+	-	-	-	+	-	+	+	-	-	-	-	-	+	+	+	46	88	47	90	47	84	45	87	65	100	4
24	55	m	11	-	+	-	-	+	-	+	-	-	-	-	-	-	+	-	-	45	89	44	86	43	83	44	85	66	98	4
25	56	m	12	+	-	-	-	+	-	+	+	-	-	-	-	-	-	-	+	44	85	44	88	45	88	43	86	67	100	4

MASTER CHART – GROUP B -2 % FUSIDIC ACID CREAM

Sl no	age	sex	dur	symptoms			morphology			site			other infns		Other skin ds		Other syst diseases			C red% day		I red % day		DC Red% day		S Red% day		W Red% day		R
				I	D	B	BR	RB	BL	A	G	IM	T	K	AC	AN	DM	H	O	7	14	7	14	7	14	7	14	7	14	
1	26	f	6	-	+	-	-	+	-	+	+	-	-	-	-	-	-	-	+	53	82	43	84	56	87	40	75	58	80	3
2	36	f	3	+	-	-	-	+	-	+	-	-	-	-	-	+	+	-	+	57	92	55	98	62	90	56	81	66	100	4
3	38	m	6	-	-	-	-	+	-	+	+	-	-	-	-	-	+	+	+	51	94	52	93	57	93	52	82	75	100	4
4	40	m	2	-	+	-	-	+	-	+	-	-	-	-	-	+	-	-	-	50	90	56	95	55	93	54	79	68	100	4
5	40	f	7	-	+	-	-	-	+	+	-	-	-	-	+	-	+	-	+	46	92	48	88	58	82	55	60	66	90	3
6	41	f	8	-	-	+	-	+	-	-	+	-	-	-	-	-	-	+	-	57	89	51	92	53	95	52	75	70	99	4
7	42	m	3	+	-	-	-	+	-	+	-	-	-	-	-	-	+	-	+	56	88	53	94	51	94	53	73	58	98	4
8	43	f	16	-	-	+	+	-	-	-	+	-	-	-	-	-	+	-	+	53	94	52	93	55	96	55	75	65	100	4
9	44	f	9	-	+	-	-	+	-	+	+	-	-	-	-	-	+	-	-	49	96	51	90	46	77	48	70	53	86	3
10	45	m	5	-	-	+	-	+	-	-	+	-	-	-	+	+	+	-	+	57	92	53	89	57	96	49	73	69	100	4
11	43	f	14	+	-	-	-	+	-	+	+	-	-	-	-	-	+	-	+	59	98	54	92	53	99	53	71	73	100	4
12	46	f	8	-	-	+	-	+	-	+	+	+	-	-	-	-	-	-	-	52	96	50	90	55	98	55	72	75	100	4
13	47	f	7	-	-	+	+	+	-	+	+	-	-	-	-	-	+	+	-	51	97	49	88	58	95	52	76	64	100	4
14	41	m	4	-	+	-	-	+	-	+	+	-	+	-	-	-	-	-	+	50	95	51	94	48	86	45	65	51	84	3
15	42	f	9	-	-	+	-	+	-	+	+	-	-	-	-	-	+	-	-	52	92	49	96	55	94	53	73	75	100	4
16	43	m	10	+	-	-	-	+	-	+	+	-	-	-	+	+	-	+	+	51	88	53	95	46	96	55	62	52	88	3
17	49	f	11	-	-	+	-	+	-	+	+	-	-	-	-	-	+	-	-	57	94	56	97	59	95	51	71	69	100	4
18	44	f	12	-	+	-	-	+	-	+	+	-	-	-	-	-	-	-	+	55	90	52	92	55	99	52	77	74	100	4
19	53	m	9	-	-	+	-	+	-	+	+	-	-	-	-	+	+	-	+	54	95	51	93	55	95	54	76	64	99	4
20	51	f	9	-	-	+	-	+	-	+	+	-	-	+	-	-	-	-	+	59	88	55	90	58	94	52	75	73	100	4
21	55	f	11	-	+	-	-	+	-	+	+	-	-	-	-	+	+	-	-	62	83	57	89	54	98	49	74	72	100	4
22	56	m	7	-	-	+	+	-	-	+	+	-	-	-	-	-	-	-	+	51	89	49	93	58	97	51	77	68	100	4
23	57	f	6	-	+	-	-	+	-	+	+	-	-	+	-	-	+	-	-	55	88	48	95	56	99	52	74	74	100	4
24	52	m	18	-	-	+	-	+	-	+	+	-	-	-	-	-	-	-	+	58	90	53	99	57	96	55	78	75	100	4
25	58	m	20	-	-	+	-	+	-	+	+	-	-	-	-	-	-	-	-	63	92	55	92	61	99	53	77	76	100	4

